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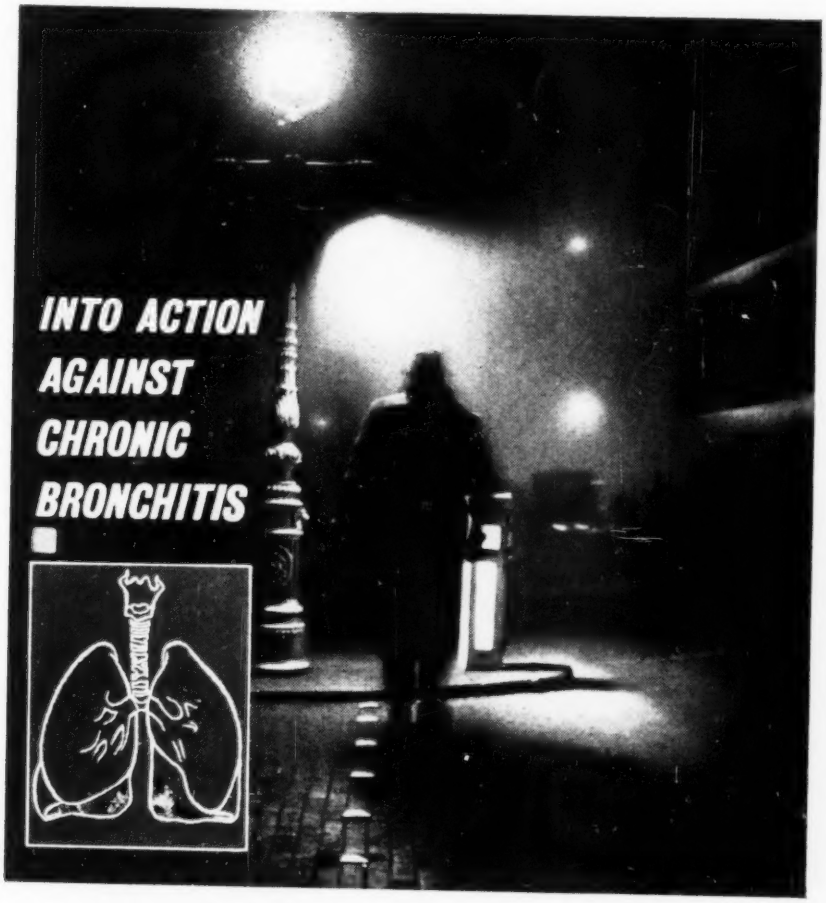

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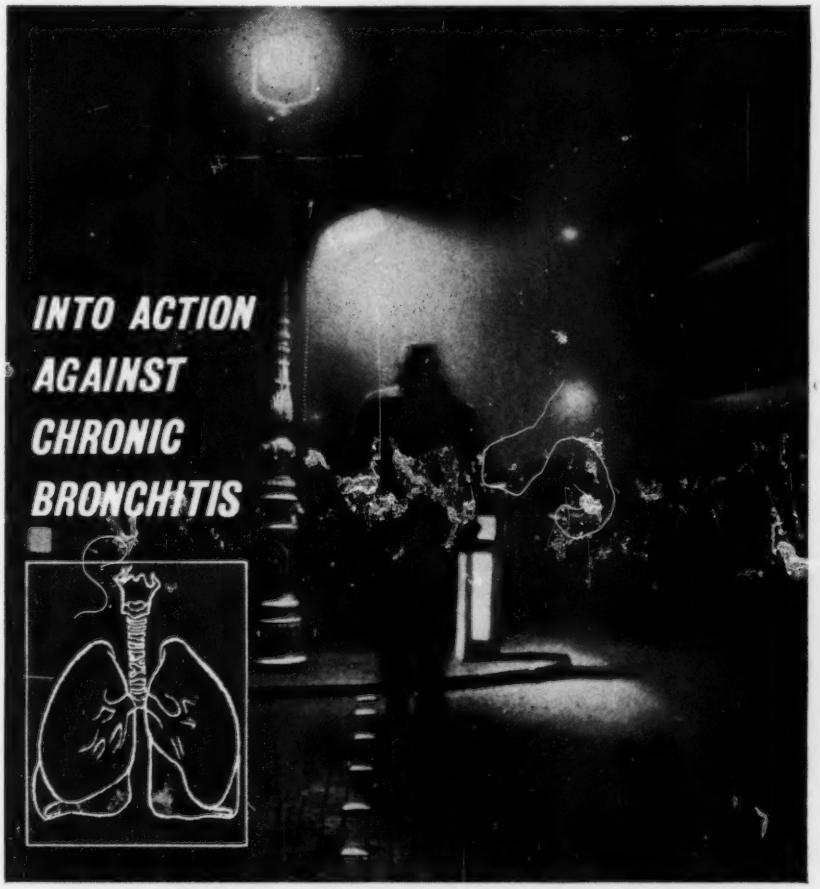

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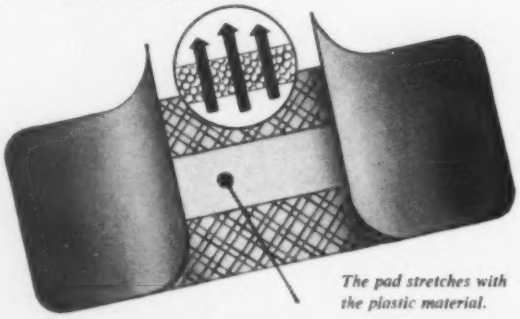

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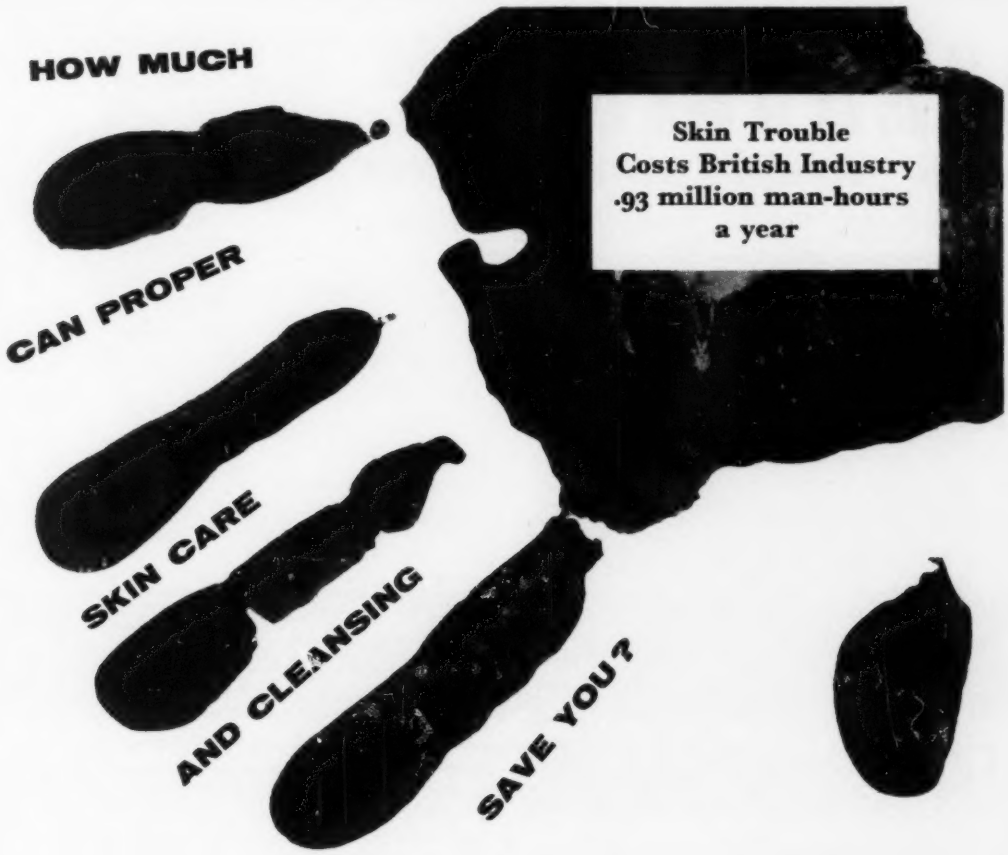

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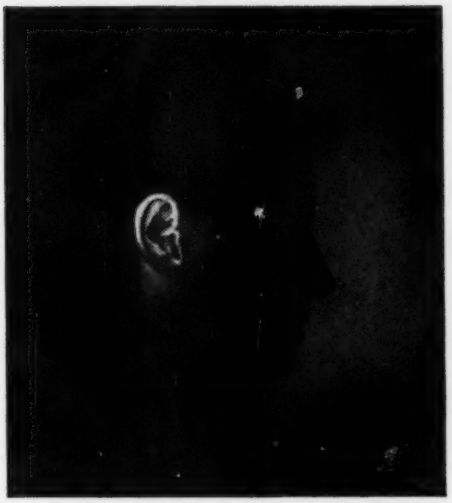

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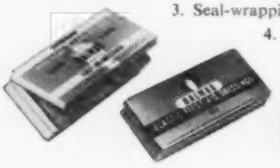

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Brit. J. industr. Med., 1958, **15**, 1.

THE TREATMENT OF EXPERIMENTAL SILICOSIS WITH COMPOUND 48/80

BY

J. MARKS, DINAH M. JAMES, and T. G. MORRIS

From the Central Tuberculosis Laboratory, Cardiff, the Department of Pharmacology, Welsh National School of Medicine and the Pneumoconiosis Research Unit, Cardiff

(RECEIVED FOR PUBLICATION JULY 24, 1957)

To treat established silicosis it would appear to be necessary to inactivate the dust in the lungs in order to prevent further toxic action and permit the repair of what damage is reversible. The drug used would presumably need to reach phagocytic cells which have transported the dust from the alveoli to the interstitial tissue and lymph nodes. In the conditions of experimental silicosis, aluminium has a protective effect (Dworski, 1955) but its administration to man by inhalation has not been proved to benefit the disease when once established (Kennedy, 1956). It is not certain that inhaled aluminium powder has the capacity to reach silica in the tissues and it is possible that soluble antagonists would prove more effective.

In an earlier communication (Marks, 1957), it was reported that compound 48/80, an organic base used experimentally as a histamine liberator, protects phagocytic cells in tissue culture against the toxic effect of silica dust. The degree of protection observed appeared sufficiently high to merit a study of the drug's activity *in vivo*. Mice were used because of their relatively low susceptibility to histamine and because a convenient technique has been described for inducing silicosis in them (Zaidi, King, Harrison, and Nagelschmidt, 1956).

Experimental Methods

Administration of Silica.—Male albino mice were used. They weighed 18 to 20 g. except in experiment 4 in which they weighed 25 to 30 g.

A single batch of tridymite dust (provided by Dr. G. Nagelschmidt, Safety in Mines Research Establishment, Sheffield) was used. It had the following size distribution:

Diameter(μ)	0·06-0·11	-0·23	-0·45	-0·9	-1·8	-3·6	-7·2
No. %	26·7	37·9	30·3	5·0	0·095	0·092	0·009

The dust was normally suspended in pyrogen-free 0·9% NaCl at a concentration of 10 mg. per ml., heated at 100° C. for 15 minutes to sterilize it, and then shaken mechanically for 20 minutes. A single dose of 0·5 ml. of suspension was given by slow injection into a tail vein. Some mice died within a few minutes of the injection. Such immediate deaths are recorded below in the text but not in the tables. Survivors of the dust injection were allotted to the experimental groups at random.

Administration of Compound 48/80.—Fresh solutions were made daily in sterile saline and given intraperitoneally in a volume of 0·3 ml. or 0·5 ml. according to the following treatment schedules.

Day	High-dose Schedule (μg.)	Low-dose Schedule (μg.)
1	10 twice	6 twice
2	20 ,,	12 ,,
3	30 ,,	18 ,,
4	40 ,,	24 ,,
5	50 ,,	30 ,,
6	50 once	30 once
7	No treatment	No treatment
8	50 once	30 once
9	55 ,,	33 ,,
10	60 ,,	36 ,,
11	65 ,,	39 ,,
12	72·5 ,,	43·5 ,,
13	80 ,,	48 ,,
14	No treatment	No treatment

When treatment extended beyond two weeks, mice on the high-dose schedule received 80 μg. and those on the low-dose schedule, 48 μg. once each day, omitting Sundays.

In two of the experiments, of which details are given below, short intensive courses of compound 48/80 were used, preceded by mepyramine to protect against the effects of histamine release.

Treatment began on the same day as the dust injections after an interval of a few hours.

Assessment of Severity of Silicosis.—Mice were killed between two and three months after having received dust. The livers were weighed before and after taking approximately 10% for section. The collagen content of the remainder of the liver was estimated by a modification (to be published) of the method of Stacy and King (1954). The collagen values given in the tables represent the content of the whole liver, allowance having been made for the portion taken for histology.

The histological assessment was made on sections

stained with haematoxylin and eosin using the following grades:—

O No structural abnormality.
A A few small collections of mononuclear cells (not more than were found in some normal mice).
B A small to moderate number of early silicotic nodules with little collagen production.
C A large number of well-developed silicotic nodules which were predominantly cellular although collagen was obvious.
D Intermediate between C and E in that some lesions were mainly cellular and others mainly collagenous.
E A large number of nodules in which collagen predominated.
F A large number of nodules, almost entirely acellular.

Intermediate gradings, denoted by a + sign, were made in some instances. In order to avoid bias in grading, the identities of specimens were not disclosed until assessment was complete.

Results

Experiment 1.—After the dust suspension was shaken, some coarse aggregations remained which were dispersed by gentle grinding in a Griffith's tube. The intravenous injection of the mice in experiment 1 appeared to be less effective than in later experiments when experience had been acquired. For example, there was only one immediate death out of 61 mice injected and only two premature deaths subsequently. Moreover, the incidence of silicosis in the untreated mice killed after two months was low as compared with later experiments. Nevertheless, the results of the initial experiment were sufficiently useful to merit description.

Of the mice surviving the dust injection, groups of six were treated with compound 48/80 for two, four, or eight weeks, using the high-dose schedule or for eight weeks using the low-dose schedule, and 12 mice were given control injections of 0·5 ml. of saline intraperitoneally, timed as in the eight-week course. The other 24 mice given dust were used for a purpose not relevant. One mouse in the low-dosage group died after 57 days and is included in the table with the two-month series. A mouse which died after 21 days on high dosage was discarded. The majority of the mice were killed two months after their dust injections but two of each treated group and four untreated mice were allowed to survive a further month. Ten control mice were not given dust but were treated with saline intraperitoneally, six being killed after two months and four after three months.

The histological and chemical observations made in experiment 1 are recorded in Table 1, the position of individual mice in the table being the same in both sections. For convenience, mice given silica but no treatment will be designated group S, those given silica and 48/80 as group ST, and controls given neither silica nor treatment, as C. The mice killed after two months afforded little information since silicosis had developed in only a minority of group S. However, all four of the group S mice allowed to survive three months developed silicosis, which was moderately severe in three. In contrast, there was only a single very mild case amongst the eight mice of group ST killed after three months. The treated mice have been assembled for analysis in group ST, irrespective of their course of 48/80, because of their small numbers. The liver collagen estimations agreed with the histological findings in demonstrating the protective effect of 48/80 in the three-month series. The mean liver collagen content after three months was 5·65 mg. in group S, 2·53 mg. in group ST, and 2·25 mg. in group C. The difference between groups S and ST is significant ($t = 5{\cdot}24$, $t_{0{\cdot}05} = 2{\cdot}23$), that between groups ST and C is not significant ($t = 1{\cdot}23$, $t_{0{\cdot}05} = 2{\cdot}23$). A similar analysis for the mice killed after two months shows

TABLE 1

EXPERIMENTAL SILICOSIS TREATED WITH COMPOUND 48/80 : EXPERIMENT 1

		Histological Grading and Liver Collagen Content						
		Given Silica (5 mg. tridymite intravenously)					No Silica	
		No Treatment	48/80 Low Dose 8 Weeks	48/80 High Dose			No Treatment	
				2 Weeks	4 Weeks	8 Weeks		
No. of animals		12	6	6	6	6	10	
Histological grading	Killed after 2 months	D B+ B O O O O O	A O O O	A O O O	O O O Died	B A O O	A O O O O O	
	after 3 months	D+ D+ D B	O O	O O	A O	A+ O	A O O O	
Liver collagen content (mg.)	Killed after 2 months	5·2 6·7 2·7 2·3 2·3 2·2 2·0 1·8	2·5 2·4 2·2 1·9	3·0 2·7 2·3 1·8	2·5 2·1 1·9 Died	2·7 2·6 2·7 2·6	2·8 2·8 3·2 2·7 2·2 2·0	
	after 3 months	7·4 5·7 6·1 3·4	2·5 2·4	3·2 1·8	2·8 2·1	2·7 2·7	2·6 2·2 2·3 1·9	

Individual mice are represented in similar places in the two sections of the table. See text for the histological grades.

TABLE 2
EXPERIMENTAL SILICOSIS TREATED WITH COMPOUND 48/80 : EXPERIMENT 2

	Histological Grading and Liver Collagen Content								
	Given Silica							No Silica	
	No Treatment	Mepyramine + 48/80		48/80 Low Dose 8 Weeks	48/80, High Dose*			No Treatment	
		2 Days	7 Days		2 Weeks	4 Weeks	8 Weeks		
No. of mice	14	6	6	6	19			6	
Deaths after admission to group	10	4	5	4	7			0	
Histological grading	D C+ C B	D D	B	B A+	C B A+	C B A O	A+ A+ A A O	. . . . . .	
Liver collagen content (mg.)	7·5 4·4 7·6 4·4	10·3 8·2	3·7	4·8 4·7	4·2 4·0 5·0	4·8 4·2 4·9 3·5	3·2 3·1 3·0 2·8 2·7	2·8 2·2 2·1	2·3 2·1 2·1

The duration of the experiment was two months.
*The three groups were not distinguished until after two weeks' treatment by which time five of the seven deaths had occurred.

no significant difference between groups S and ST ($t = 1{\cdot}60$, $t_{0{\cdot}05} = 2{\cdot}08$) or between groups ST and C ($t = -1{\cdot}23$, $t_{0{\cdot}05} = 2{\cdot}09$).

Experiment 2.—The silica dust was prepared and administered as in experiment 1. The greater effectiveness of the injection with experience was confirmed by an immediate mortality of seven out of 58 mice given dust, the loss of a further 30 before the experiment ended, and the development of silicosis in two months in all the mice given dust without treatment. Two additional treatment schedules were introduced in experiment 2. The dose of 48/80 used was 50μg. intraperitoneally twice daily for two days in one schedule and for seven days in the other, each dose preceded by 100 μg. of mepyramine given subcutaneously 20 minutes earlier. The purpose of the mepyramine was to diminish the toxicity of 48/80 in short intensive courses.

Deaths were frequent in the mice given dust whatever their group. Most occurred in the first two weeks and especially in the first seven days. There were five deaths amongst 19 mice receiving the high-dosage schedule by the time allotments were made to the two-, four-, and eight-week treatment groups at the end of two weeks' treatment. Four (1), four (0), and six (1) mice were allocated respectively to these three groups, the number of deaths subsequently being given in parenthesis. The total loss of seven mice out of 19 treated with the high-dose schedule compares favourably with the loss of 10 of 14 mice given silica without treatment (group S). The mortality in the other treatment groups was about the same as in group S.

Surviving mice were killed two months after the injections of dust. The results of their examination are given in Table 2. With both methods of assessment it was evident that the mice given the eight-week high-dose schedule of 48/80 (to be called group ST8) were considerably protected against the effects of silica. A slight degree of protection appeared to be given by the same schedule continued for only two or four weeks but survivors in the other treatment groups were too few to be useful. The mean liver collagen content was 5·97 mg. in group S, 2·96 mg. in group ST8, and 2·27 mg. in group C (no silica). The difference between groups S and ST8 is significant ($t = 3{\cdot}74$, $t_{0{\cdot}05} = 2{\cdot}37$). That between groups ST8 and C is also significant ($t = 4{\cdot}69$, $t_{0{\cdot}05} = 2{\cdot}26$), showing that the protection conferred on group ST8 was not complete.

Experiment 3.—For this experiment the dust was lightly ground in saline in a glass tissue grinder ("dewarex" brand) and dextran solution then added to give a final concentration of 4·5% dextran and 10 mg. dust per ml. The modification (suggested by Dr. D. Rivers) was introduced in an attempt to reduce the lethal effect of the dust injections by providing a finely dispersed suspension slow to settle out. Later investigation of tissue grinders of the type used indicated that the toxicity of silica dust ground in them may be reduced by contamination with metal, *e.g.*, iron, used in their manufacture. In the event, the mortality in experiment 3 was somewhat lower than that in experiment 2 which had been carried out concurrently with the same stock of mice. There were three immediate deaths amongst the 52 mice injected with dust and 18 others during the course of the experiment, which was ended after 11 weeks.

The control mice (group C) were common to the concurrent experiment 2 but will not be further

TABLE 3

48/80 : EXPERIMENT 3

	Histological Grading and Liver Collagen Content							
	No Treatment		48/80 High Dose*					
			2 Weeks		4 Weeks		8 Weeks	
No. of mice	14		12		12		11	
Deaths after admission to group	4		5		5		4	
Histological grading	E+ E D+ D C+	E E D C+ C	E D C B	E C+ C	C+ C B+ A	C C B+	C A O O	B+ A O
Liver collagen content (mg.)	10·2 14·3 12·1 12·2 10·1	23·1 19·3 15·1 14·6 5·7	13·1 7·9 7·6 4·1	10·1 8·3 6·9	5·6 6·3 4·6 2·8	6·4 5·6 4·1	3·7 5·0 5·8 4·1	6·1 4·4 5·0

All mice represented in the table received silica.
*The duration of the experiment was 11 weeks.

considered as they were killed after only two months.

The incidence of deaths, the histological findings, and the collagen values in experiment 3 are recorded in Table 3. It is apparent that 48/80 offered no protection against the lethal effect of the silica. Histologically, protection by 48/80 was clearly evident with the four- and eight-week courses (groups ST4 and ST8 respectively) but was not obvious with the two-week course (group ST2). However, all three treated groups had lower mean liver collagen values than the untreated mice given silica (group S), the differences observed being significant ($t = 4{\cdot}65$, $4{\cdot}49$ and $2{\cdot}61$ for comparisons of group S with groups ST8, ST4, and ST2 respectively, $t_{0{\cdot}05}$ being $2{\cdot}13$). The collagen values for the livers of mice given silica in experiment 3 (and also in experiment 4) were somewhat higher than those for livers with comparable histological gradings in experiments 1 and 2, although the technique of examination was the same. Whatever the cause of the disparity it does not affect comparisons made between the groups in each experiment.

Fig. 1 is a section of the liver of an untreated mouse (group S) histologically graded E+ (collagen 10·2 mg.). It was stained by Mallory's trichrome method, the collagen showing as lighter areas. Fig. 2 is a similarly stained section of the liver of a mouse treated for eight weeks (group ST8) histologically graded O (collagen 4·1 mg.). Fig. 3 is a section of a liver graded E (collagen 19·3 mg.) from group S, stained by Van Gieson's method, the darker areas representing collagen, and Fig. 4 is a section similarly stained of a liver graded O (collagen 5·8 mg.) from group ST8. Fig. 5 is a composite one of silver-impregnated sections of all livers in group S, showing reticulin formation. From left to right their

FIG. 1.—Experiment 3: silicosis of liver in tridymite-injected mouse given no treatment. Mallory's trichrome stain, blue-sensitive plate. ×60.

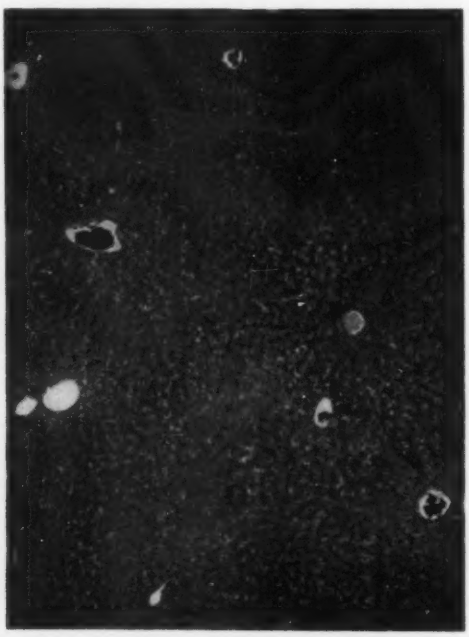

FIG. 2.—Experiment 3: liver of tridymite-injected mouse treated with a high-dosage schedule of 48/80 for eight weeks. Stained as for Fig. 1. ×60.

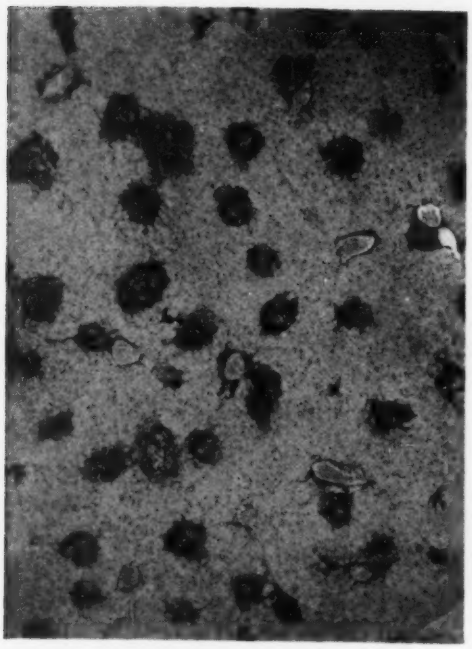

FIG. 3.—Experiment 3: silicosis in liver of tridymite-injected mouse given no treatment. Van Gieson's stain. ×55.

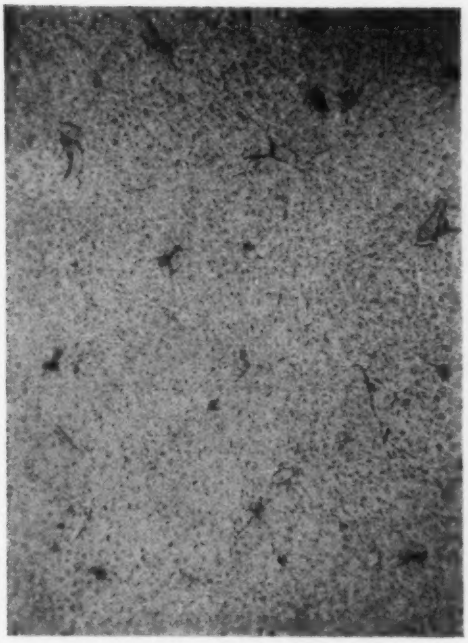

FIG. 4.—Experiment 3: liver of tridymite-injected mouse treated with a high-dosage schedule of 48/80 for eight weeks. Van Gieson's strain. ×55.

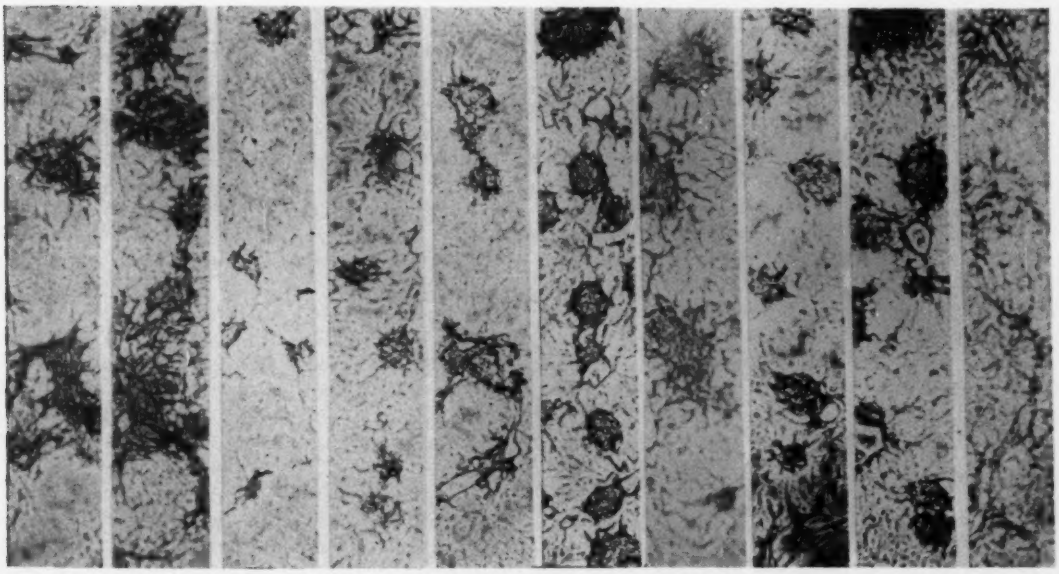

FIG. 5.—Experiment 3: livers of the 10 tridymite-injected mice given no treatment. Silver impregnation for reticulin. ×55.

TABLE 4

EXPERIMENTAL SILICOSIS TREATED WITH COMPOUND 48/80 : EXPERIMENT 4

	Histological Grading and Liver Collagen Content											
	Given Silica										No Silica	
	No Treatment		Mepyramine and 48/80 3 Days		48/80, High Dose						No Treatment	
					2 Weeks		4 Weeks		8 Weeks			
No. of mice	25		13		11		12		11		6	
Deaths after admission to group	19*		6		4		5		3		0	
Histological grading	F	D	C+	C	D	C+	D	C	B+	B+	. .	
	D	D	C	B+	C	C	C	C	B	A+	. .	
	D	C+	B	B	C	C	B	A+	A+	A	. .	
	C		O		B		A		A	O		
Liver collagen content (mg.)	11·9	18·8	10·8	9·6	8·2	11·7	5·0	8·3	7·7	6·1	3·0	2·5
	17·0	15·5	4·6	9·0	9·3	8·2	5·9	5·6	3·9	4·8	2·3	2·3
	15·2	lost	10·5	7·4	7·5	5·5	5·7	3·7	3·5	5·9	2·3	lost
	12·9		3·8		4·2		5·4	5·1	3·9			

The duration of the experiment was two months.
*A mouse which died one day before the end has been included (histology grade F, collagen 11·9 mg.).

histological gradings on haematoxylin-and-eosin-stained preparations were C+, E, C, E, C+, E, E+, D, D, D+ and collagen values 14·6, 23·1, 5·7, 14·3, 10·1, 19·3, 10·2, 12·2, 15·1, 12·1 mg.

Experiment 4.—The dose and preparation of the dust were the same as in experiment 1 but larger mice (25 to 30 g.) were used in an attempt to reduce their mortality. Nevertheless, there were 11 immediate deaths amongst 83 mice injected with dust. Five others were very sick and were discarded, and, of the remainder, 37 died during the course of the experiment which lasted two months. Four groups of the mice given dust were treated with 48/80, three receiving the high-dose schedule for two, four, or eight weeks and the fourth, 50 μg. doses twice daily for three days. Mepyramine, 200 μg., was given subcutaneously 20 minutes before each dose of the three-day course of 48/80. Six control mice were given neither silica nor 48/80.

The incidence of deaths and the histological and chemical findings are shown in Table 4. The lethal effect of silica appeared to be reduced by treatment with 48/80 and it was clear that, given at the high dosage level for eight weeks, the drug conferred considerable protection against silicosis. Shorter courses of treatment were less effective but afforded some protection even with the period limited to three days. The collagen values for each of the treated groups were significantly lower than for the mice left untreated after receiving silica, as the following results show:—

Treatment	Nil	Three Days	Two Weeks	Four Weeks	Eight Weeks
Mean collagen (mg.)	15·22	7·96	7·80	5·66	5·11
t (comparison with untreated group)	—	4·85	5·34	8·61	9·52
$t_{0.05}$	—	2·20	2·20	2·20	2·18

The eight-week course of 48/80 treatment was not completely protective, however, either by histological or chemical criteria. Collagen values for mice on this course were significantly higher than for the controls ($t = 4{\cdot}05$, $t_{0.05} = 2{\cdot}20$).

Discussion

The chief value of the observations described above would appear to lie in their demonstration that it is possible for a drug given systemically to reach and inactivate toxic silica dust in the tissues of an animal. Jäger and Müller (1956) have claimed a similar effect for a protective agent but give no account of its chemical nature and the method they used to assess protection lacked precision. Although compound 48/80 has been administered to man (Nordlander, 1957), its toxicity precludes consideration of its use in the treatment of silicosis. Investigation into the relation between silica neutralization by organic bases and their histamine-releasing activity is needed in order to ascertain whether any can be found which are suitable for therapeutic trial.

Although the experiments described have clearly demonstrated the protective power of compound 48/80 against silicosis, it appears in retrospect that the dose of tridymite used may have been somewhat greater than the optimum for the display of the antagonists' activity. In experiments 2 and 4 the dose of silica used resulted in a very high death rate in the untreated mice, although in compensation the protective effect of 48/80 against the lethal effect of the dust was well displayed. The results presented in the tables show broad agreement between the histological and biochemical methods used to assess the degree of liver silicosis although there were discrepancies in some individual cases.

Information is not available at present as to the rate at which 48/80 is destroyed or excreted. In further work on screening drugs for use in silicosis it would perhaps be advantageous to select for examination compounds which are not readily metabolized, because the toxic action of silica appears to be maintained *in vivo* for a considerable time if not permanently.

Summary

Mice were given silica dust (tridymite) intravenously and the amount of silicosis induced in the liver assessed by histological examination and by estimation of the liver collagen content. A considerable degree of protection against the effect of the dust was obtained by treating the mice with compound 48/80, an organic base previously shown to be effective *in vitro*.

We are indebted to Professor J. Gough, Dr. G. Nagelschmidt, and Dr. D. Rivers for advice during the course of this work or on its presentation and to Dr. E. Lewis-Faning for the statistical analyses. Mr. C. A. Lediard prepared the sections and photographs.

References

Dworski, M. (1955). *A.M.A. Arch. industr. Hlth.* **12**, 229.
Jäger, R., and Müller, J. (1956). *Beitr. Silikose-Forsch.* Special Issue "Grundfragen aus der Silikoseforschung." Bochum 1956, p. 105.
Kennedy, M. C. S. (1956). *Brit. J. industr. Med.*, **13**, 85.
Marks, J. (1957). *Ibid.*, **14**, 81.
Nordlander, N. B. (1957). *Acta med. scand.*, **157**, 235.
Stacy, B. D., and King, E. J. (1954). *Brit. J. industr. Med.*, **11**, 192.
Zaidi, S. H., King, E. J., Harrison, C. V., and Nagelschmidt, G. (1956). *A.M.A. Arch. industr. Hlth.* **13**, 112.

Brit. J. industr. Med., 1958, **15**, 8.

IMMUNOLOGICAL FACTORS IN THE PATHOGENESIS OF THE HYALINE TISSUE OF SILICOSIS

BY

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Several hypotheses have been suggested in explanation of the pathogenesis of silicosis. The earliest was the mechanical hypothesis, according to which, quartz particles, being pointed and sharp, would irritate the cells, stimulating their proliferation. This hypothesis was discarded when it was seen that other minerals, with edges even harder and sharper than quartz, such as carborundum and diamond, did not produce fibrosis. In 1922 Gye and Purdy put forward the chemical theory. They suggested that silicic acid, on being slowly released by crystalline silica, would react as a toxic substance capable of inducing fibrosis. This hypothesis was long held, and until a short time ago it was supported and expanded by King (1947) and his colleagues. It was never clearly established how the dissolved silicic acid actually produced fibrosis. It was believed by some that monosilicic acid was the fibrogenic agent, and by others that it was polymerized silicic acid. However, no conclusive evidence has been produced to show that the dissolved silica induces fibrosis and by what means, and this is true also for the interesting hypothesis, recently put forward by Kikuth (1956), which focuses attention on the damage which monomeric silicic acid may exert on some cellular structures (mitochondria).

In the last 10 years several physical hypotheses have been proposed: the piezoelectric (Velicogna, 1946; Evans, 1948) and radioactivity of quartz theories (Dantin-Gallego, 1948), both found unacceptable by Parmeggiani (1950), and also the most interesting and impressive hypothesis formulated by Jäger (1954) and Seifert (1954) in which they suggested that the crystalline lattice surface of the quartz would act as a matrix on which cellular proteins would reform and consequently be denatured. The reforming of the proteins would cause them to assume the shape and properties of fibrous proteins, hence the capacity of free crystalline silica for producing fibrous tissue. This theory is supported by the fact that amorphous silica is far less fibrogenic than crystalline silica (Rüttner, Willy, and Baumann, 1954).

The arguments on the solubility hypothesis and on the physical hypothesis of the action of surfaces led to numerous additional investigations. In an excellent critical paper, King, Zaidi, and Nagelschmidt (1956) summarized and discussed all the points for and against the theory of solubility. The facts which contradict the validity of this theory as originally stated are the discrepancy between the solubility of various forms of free silica and their fibrogenic action, and the improbability that there is polymerized silicic acid in the tissues. King himself arrived at the conclusion that the solubility of the silica could not serve itself to explain the pathogenesis of silicosis.

Jäger has ably illustrated the points in favour of the theory of surface action. However, he did not succeed in explaining why certain non-crystalline forms of silica, such as condensation silica (Policard and Collet, 1954), have some fibrogenic action. Jäger also has not explained why areas of massive fibrosis are formed, nor why other mineral dusts alone or in combination with a small percentage of quartz can, in certain conditions, cause massive fibrosis.

It must be remembered that the hypotheses of chemical action and surface action were intended more to define the aetiological agent rather than the pathogenic mechanism of silicosis. They state that it is either dissolved silicic acid or silica crystals as such which cause fibrosis; but how these factors actually induce the formation of this particular hyaline fibrous tissue of silicosis has never been satisfactorily explained. The theory of Holt and Osborne (1953) that polymerized silicic acid acts like mucopolysaccharides, facilitating and directing the formation of fibrils and hence the production of collagen, and the one proposed by Jäger that connective tissue formation would be induced directly by a fibrous transformation of proteins

absorbed on the crystalline lattice of quartz are not convincing. If it were, in fact, so, it still would be difficult to explain the varieties, extension, and evolution of silicotic fibrous tissue, and particularly the peculiar type of hyaline and its capacity for originating confluent masses, whose dimensions are out of proportion to the surface of quartz crystals which may be found in them.

The failure of mechanical, chemical, and physical theories to explain the pathogenesis of silicosis, and the belief that (Vorwald, 1950) inborn or acquired peculiarities of the subject may influence the beginning and development of this disease have prompted other approaches to the pathogenic problems. Policard, Croizier, and Martin (1937) and others have, for a long time, emphasized the importance of the tubercular factor, considering it indispensable in the genesis of silicotic nodules. Others (Cummins, 1940 and others) have affirmed that massive fibrosis is induced by the combined action of quartz and Koch bacilli, but they have not explained why and how this happens. In the last few years several investigators (Scheel, Smith, Van Riper, and Fleisher, 1954; Webster, 1956; Koch, 1949; Claeys, 1954) have suggested that the intervention of an immunological factor should be considered in relation to silicosis, and some of them have sought to demonstrate the antigenic properties of free silica; Antweiler and Hirsch (1956) with aerosil and Claeys with quartz reported negative results. But Scheel *et al.* (1954) succeeded in demonstrating that quartz coated with serum proteins and injected into the rabbit elicits the production of antibodies. Up to the present time it can be said that the belief that immunological factors play a rôle in the pathogenesis of silicosis has not been supported by any conclusive evidence.

We have been convinced from the first of the importance of the specific reaction of the host organism in the pathogenesis of silicosis, and have developed our research work in this direction. It has led us to believe that the immunological hypothesis is, at the moment, the only one which is able to explain the formation of hyaline nodules and fibrous tissue masses. Our guiding idea derives from the belief at the present time that an immunological pathogenesis is at the base of many so-called collagen diseases*, and in particular of rheumatoid arthritis, lupus erythematosus, periarteritis nodosa, and scleroderma. Silicosis can be considered, from many points of view, as a collagen disease.

* We use the term "collagen disease" because it is now widely used to define the group of diseases having in common that the connective tissue is involved to a smaller or greater extent. In fact, we are aware that this term is inappropriate since it is based on an element of the connective tissue, the collagen fibrils, which definitely do not partake in the pathological process.

The Blood Protein Changes of Silicosis

In 1950, Vigliani, Boselli, and Pecchiai recognized that in silicotic patients the blood proteins were almost always changed because of the increase in gamma globulins, and in cases with additional infections, also in alpha and beta globulins. This finding was confirmed by several investigators. All those who used a suitable technique have confirmed that in silicosis there is almost invariably an increase of serum gamma globulins and sometimes also of beta and alpha globulins. The blood protein changes in silicosis are associated with an increase in globulin-producing parenchymal cells in certain sites.

It is well known that antibodies belong mostly to the gamma globulin group; therefore, the increase in gamma globulins in silicosis might be either the expression of an increased antibody production or of an increase of gamma globulin production parallel to the production of antibodies (see Boyd and Bernard, 1937). In fact, changes in blood proteins similar to those found in silicosis are found in all the conditions of hyperimmunization and in all the collagen diseases. It is true, however, that serum gamma globulins are increased also in a wide variety of diseases not necessarily connected with an immunity reaction, and as yet it has not been established that the increased gamma globulins of silicotics are totally or in part antibodies.

The Chemical Composition of Hyaline Tissue in Silicosis

In our Institute, Pernis (1954, 1955), Pernis and Ghislandi (1956), and Pernis and Clerici (1957) have demonstrated that silicotic hyaline tissue differs in many respects from other physiological and pathological hyaline tissues such as that of scar tissue. True connective hyaline tissue is composed almost entirely of collagen fibres (Letterer, Gerok, and Schneider, 1955), but silicotic hyaline consists of 40% collagen, the remainder being globulin which must be considered as having an intermediate position between serum beta and gamma globulin. Silicotic hyaline tissue also contains carbohydrate in quantities of about 3% of the total amount of the proteins, and lipids corresponding to 20%.

From a biochemical point of view (see Table 1), the silicotic hyaline tissue is very similar in its globulin, carbohydrate, and lipid content to amyloid substance. The so-called silicotic hyaline, then, consists of a reticular structure, within which serum globulins have precipitated. Indeed, very recently Pernis, Ceppellini, and Ghezzi (1957) demonstrated immunologically the presence of serum globulin in the hyaline tissue of silicosis. They isolated the hyaline tissue from pulmonary silicotic nodules freshly obtained at necropsy and homogenized the

TABLE I
CHEMICAL COMPOSITION OF HYALINE TISSUES OF SILICOSIS AND PERISPLENIC SYNECHIAE COMPARED WITH THAT OF LUNG AMYLOID FROM A CASE OF PRIMARY AMYLOIDOSIS

Tissue	Proteins (% total protein)		Carbohydrates (g./100 g. protein)				Lipids (g./100 g. protein)	
	Collagen	Globulins	Hexuronic Acids	Hexosamines	Hexoses	Methylpentoses	Total Lipids	Cholesterol
Hyaline tissue of silicosis	40·2	59·8	0	0·58	2·13	0·28	20·1	3·72
Hyaline tissue of perisplenic synechiae ..	82	18	0	0·26	1·04	0·31	3	0·30
Lung amyloid ..	41·2	58·8	0	1·12	2·20	0·36	14·3	3·60

tissue; the resulting suspension was then washed and re-homogenized six times in saline, in order to eliminate all traces of blood or lymph, and injected intraperitoneally into rabbits. The antisera which were obtained reacted with normal human serum electrophoretically separated in an agar plate after the technique of Grabar and Williams (1955), giving a single line of precipitation extending through the zones of beta and gamma globulins.

A similar result was obtained by reversing the procedure, that is, by absorbing a rabbit antiserum against whole normal human serum with homogenized and washed hyaline tissue of silicosis and afterwards using the absorbed antiserum in an immunoelectrophoresis experiment against whole normal human serum electrophoretically separated in an agar plate. Thus, after absorption with the hyaline tissue of silicosis but not with normal human lung, it could be seen that the long line of precipitation, which normally extends through the zones of beta and gamma globulin, had completely disappeared. The other lines of precipitation were unaffected by either absorption. It appears therefore that the hyaline tissue of silicosis contains a protein antigenically related to a serum protein whose electrophoretic mobility is that of beta or gamma globulin. In this connexion it is interesting to note that Williams and Grabar (1955) have shown that serum antibodies belong precisely to this fraction.

The immunological pathogenesis of amyloid has been accepted by many pathologists (Letterer, 1949; Koletsky and Stecher, 1939; Jaffé, 1926; Teilum, 1948; Jones and Frazier, 1950) who consider that the globulin content of this substance results from antigen-antibody precipitation localized in certain tissues. This concept has been recently supported also by immunohistochemical studies (Vazquez and Dixon, 1956). Thus, the presence in silicotic hyaline tissue of a large proportion of globulin, with characteristics intermediate between those of beta and gamma, makes it possible to consider this substance as similar to amyloid, that is, as an antigen-antibody precipitate.

In addition, the existence of a large quantity of lipids in silicotic hyaline tissue agrees with this interpretation; for example, Horsfall and Goodner demonstrated as long ago as 1936 that antigen-antibody precipitates may contain a proportion of co-precipitated lipids varying from 4% to 50% of the proteins.

The Action of the Tubercle Bacillus and its Products on the Development of Human and Experimental Silicosis

It has been known for decades that in the presence of a tubercular factor silicosis follows a more rapid and malignant course with a tendency for the nodules to condense and become confluent. Thus, these cases show a rapid increase in the production of fibro-hyaline tissue in the form of masses which sometimes become pseudotumoral and do not radically differ in microscopical structure from isolated silicotic nodules save for being more cellular. Neither do these masses show any substantial differences in chemical analysis, nor do they assume the histological characteristics of tubercular tissue, unless at a very late stage and then only in part.

So-called " infective silicosis " and " progressive massive fibrosis " have been considered as silicosis and anthracosilicotic pneumoconiosis which have been modified by the action of the Koch bacillus.

Until now, a satisfactory explanation has never been given for the mechanism by which the tubercular infection modifies silicosis and coal-miner's pneumoconiosis and produces a progressive confluent or massive fibrosis. This action can be explained by postulating an immunological pathogenesis of the formation of silicotic fibro-hyaline tissue. In 1942 Freund and McDermott showed that the immunological response to the introduction of a certain quantity of antigen can be greatly enhanced if the antigen is introduced into the host organism together with a certain amount of oily emulsion containing dead tubercle bacilli, the so-called " Freund's adjuvant ". The technique of potentiating the antigen by associating it with dead tubercle bacilli has often been employed by immunologists and is found to be particularly useful in experimental auto-immunization. Assuming that quartz is capable, when introduced into the organism, of

producing antigens by itself, or by modifying proteins or polysaccharides, these antigens would be greatly potentiated by the simultaneous action of tubercular antigens, and the production of antibodies would be consequently much greater, and a more extensive precipitation of the antigen-antibody complex in the form of hyaline would be expected.

The results of some animal experiments performed by Attygalle, Harrison, King, and Mohanty (1954) might in fact be due to the adjuvant action of dead tubercle bacilli. They observed that the fibrogenic activity of different dusts (anthracite, mine dust, kaolin) could be enhanced by the simultaneous administration of 5 mg./kg body weight of dead B.C.G. The fact that dead tubercle bacilli had the same enhancing effect on fibrosis in certain animals susceptible to tuberculosis (guinea-pigs) as well as in those highly resistant to it (rats), might be interpreted as a consequence of an unspecific boosting action of the dead tubercle bacilli rather than as a consequence of a tubercular infection. It is interesting that the doses of dead tubercle bacilli used by Attygalle and his colleagues were of the same order of magnitude as those contained in the doses of Freund adjuvant used in experimental immunology. Of course, we do not mean that tubercular infection by living tubercle bacilli could not enhance the fibrogenic action of different dusts, as this has been very convincingly shown by later experiments of Zaidi, Harrison, King, and Mitchison (1955), but we suggest that in either case at least a part of the action of tubercle bacilli in enhancing fibrosis might be due to an increased immune response after the liberation in the lung tissue of some components of the tubercle bacillus (amongst these, waxes have the highest adjuvant activity).

Late Appearance of Hyaline in Experimental Silicosis

In experimental silicosis the primary lesions are reticular nodules composed of macrophages, fibroblasts, and reticular fibrils. Typical silicotic hyaline never appears earlier than 40 days after the introduction of the dust even when the dust used is of the most fibrogenic type, such as quartz washed with hydrofluoric acid or tridymite. With the quartz generally used and probably still covered by the amorphous layer, the hyaline tissue appears after a period of six or more months, depending on the mode of introduction and the quantity used. One may therefore speak of the delay in the appearance of hyaline tissue in silicosis. The minimum period of delay (40 days) is equal to the time necessary to obtain a good production of antibodies in an animal injected with antigens of various types. The latent period in the appearance of silicotic hyaline is thus consistent with the hypothesis that the hyaline is the result of an antigen-antibody reaction.

Capacity of Certain Dusts other than Quartz to Produce Massive Fibro-hyaline Tissue

It has been maintained by many people that true pulmonary pneumoconiotic fibroses are only produced by dusts containing crystalline free silica or asbestos.

Recently Hale, Gough, King, and Nagelschmidt (1956) described six cases of massive fibrosis due to the inhalation of apparently quartz-free kaolin dust. The protein composition of the hyaline tissue from one of these cases of kaolinosis, in which death was due to massive pneumoconiosis, was determined in our Institute by Pernis, who showed that the hyaline material was very rich in globulins (73%) and relatively poor in collagen (27%); morphologically the picture was practically identical with that of massive silicosis. In our opinion, the cases of massive kaolinosis can be explained, assuming that under certain conditions, *e.g.*, in chronic, torpid tubercular infection, certain dusts other than quartz may induce or increase an antibody reaction with antigen-antibody precipitation at sites of dust deposits. Kaolin has been known for some time as a good adjuvant to immune reactions.

The facts so far mentioned fit the hypothesis of the immunological genesis of fibro-hyaline tissue of silicosis and progressive massive fibrosis. If one accepts that the hyaline results from an antigen-antibody precipitate where the antigen is produced by the action of dust alone, or of dust plus an infection, it is easy to explain the formation of silicotic nodules and fibrous masses. It also explains the slow progressive course of the disease even after cessation of exposure to the dust, the aggravating and potentiating effect of infection, particularly that of tuberculosis, the occasional capacity of dusts, generally considered to be capable of producing little or no fibrosis, to induce the formation of hyaline tissue, and the variations of the individual reaction to inhalation of dust.

On the other hand objections can be made to the immunological hypothesis of silicosis, principally the following.

Absence of Typical Allergic Reactions.—This objection is not valid if one supposes that in silicosis there is a slow and continuous production of antigens and a consequent continuous desensitization. Antibodies are produced without allergic symptoms (*e.g.*, eosinophilia, or symptoms of anaphylactic shock, etc.) in animals continually injected with antigens for the production of antisera.

Production of Silicosis after Relatively Large Quantities of Quartz.—If silicosis were an allergic

disease, the small quantities of quartz inhaled physiologically should be sufficient to produce it; however, it is essential to remember that in our concept silicosis is an immunological but not an allergic disease. The analogy of silicotic hyaline and of amyloid suggests that silica (and therefore antigen) must be introduced in considerable amount, concentration, and duration in order to produce the disease. Similarly, in experimental amyloidosis produced with casein-Na, repeated and relatively large doses of this heterogeneous protein are necessary.

Lack of Serological Data Characteristic of Auto-antibody Diseases.—Serological signs, considered typical of auto-antibody diseases, such as increased haemolysis, false positive Wassermann reactions, positive Coombs and cold agglutinin tests, are not normally observed in silicosis. It can be pointed out that these signs appear only in syndromes due to antibodies against blood cells and in those with a rather acute course. Silicosis is a disease localized in the lungs and neighbouring glands and follows a comparatively slow course. Also Saita and Arrigoni Martelli (1956) have recently shown the presence of cold agglutinin up to 1 in 60 in titre and an increase in the anticomplementary activity in the serum in a certain percentage of silicotic patients.

Capacity of Silica to Induce Auto-antigens and Antibodies.—Some experiments on the capacity of silica to induce the formation of auto-antigens and auto-antibodies have given negative results. Friedberg and Lendle (1956) as well as Antweiler and Hirsch (1956) did not succeed in inducing the formation of auto-antigens and auto-antibodies in guinea-pigs and rabbits injected with colloidal silicic acid, for colloidal silica does not produce true silicosis. On the other hand, Scheel and his colleagues did succeed in obtaining the formation of anti-protein auto-antibodies with crystalline silica.

Suggested Hypotheses

If silicosis is to be considered as a disease with an immunological pathogenesis, it may be interesting to speculate as to how free silica might provoke or increase the formation of antigens and consequently of antibodies. Silica might act in the following ways: (1) Silica itself might act as an antigen. (2) Silica might induce the formation of auto-antigens. (3) Silica might act as a booster of hetero-antigens. (4) Silica might induce the liberation of auto-antigens indirectly by killing a comparatively large number of cells. These hypotheses must be discussed in the light of our limited present knowledge.

Silica Itself an Antigen.—A crystal of free silica might have antigenic properties because of its particulate nature and its specific crystalline structure. However, the attempts of Claeys to demonstrate anti-silica antibodies in the serum of silicotic patients were not conclusive. The fact that hyaline tissue is found even at a considerable distance from the quartz crystals might be explained by assuming that colloidal silicic acid is the antigen; however, the presence of highly polymerized colloidal silica in pulmonary interstitial tissue is considered uncertain, and, by some investigators (Paterson and Wheatley, 1955), even improbable. Researches by Antweiler on the antigenic properties of aerosil have given negative results.

Silica Inducing Auto-antigens.—Silica could induce the production of auto-antigens from proteins or polysaccharides. It is well known that quartz adsorbs proteins and that the adsorbed proteins can easily be denatured, and there could theoretically be three adsorption patterns of proteins on particulate matter: (1) Simple adsorption, (2) adsorption with denaturation, (3) adsorption with denaturation and specific rearrangement of protein molecules after a particular model of crystalline lattice.

It is clear that the production of auto-antigens would be facilitated most by the formation of proteins denatured according to the third pattern, which is actually what would occur according to Jäger and Seifert's hypothesis. That theory is based on the possibility of the quartz surface producing a specific altered protein on the crystal surface. With or without this specific rearrangement postulated by Jäger, the proteins adsorbed by quartz surfaces might be denatured and thus act as auto-antigens. Scheel and his colleagues (1954) have investigated whether quartz denatures proteins in such a way as to form auto-antigens and appear to have been able to demonstrate that this in fact does happen after intravenous injections in the rabbit of quartz covered with homologous serum proteins; this does not occur with other dusts.

Holzapfel (1952) recognized that certain carbohydrates, and in particular galactose, have a marked tendency to be adsorbed on quartz. The absorption of certain tissue polysaccharides on silica crystals could give them auto-antigenic properties.

Silica as a Booster of Hetero-antigens.—If one considers quartz as an antigen on its own account, or as being capable of producing auto-antigens, the Koch bacillus would act in human as well as experimental pneumoconioses as a Freund adjuvant. The " Freund adjuvant " is actually formed of dead tubercle bacilli emulsified in " aquaphor " and paraffin oil and it is used to potentiate a numerous series of antigens and auto-antigens in experimental immunology.

Also it is known that some finely powdered dusts may increase the immunological response to different antigens. Those most often used for this purpose are $AlPO_4$, $Al_2(SO_4)_3$, kaolin and other mineral dust having marked adsorbent properties. This action is probably due to their capacity for adsorbing antigens, which are therefore kept in a high local concentration and then diffuse slowly; more antibodies are thus produced, compared with antigens which diffuse rapidly (and are thereby diluted) in blood and body fluids. It is possible that the ability of these mineral dusts to cause macrophagic granulomata at the site of inoculation plays a rôle in determining an increase of the antibody response. Aluminium phosphate has been shown by King, Harrison, Mohanty, and Nagelschmidt (1955) to produce a mild fibrosis in the rat lung.

Quartz, whose crystalline lattice is identical with that of $AlPO_4$, might conceivably have the property of increasing the antibody response to different exogenous antigens which reach the zone of the silicotic granuloma. This might even occur with tubercular antigens; thus it would not be the tubercle bacillus but quartz itself acting as a booster. It is possible, however, in this case that both quartz and the tubercle bacillus act as boosters and as sources of antigens at the same time, thus potentiating each other and producing a large increase in antibody response.

The possibility that some mineral dusts might, after their penetration in the lung, act as boosters of antigens of bacterial origin might explain some cases of massive fibrosis after inhalation of large amounts of kaolin; King *et al.* (1955) were able in animal experiment to produce a pulmonary fibrosis by means of kaolin and killed tubercle bacilli, and are of the opinion that the synergistic action of kaolin and tubercle bacilli might be the cause of the cases of massive fibrosis observed in kaolin workers by Hale *et al.* (1956).

Indirect Liberation of Auto-antigens by Silica.—This has been suggested to us by Dr. Klosterkötter; it is in accord with the observation that the amount of fibrohyaline tissue generally shows a rough parallelism with the number of cells which have been damaged by quartz. Jötten and Klosterkötter (1952) have stated that in the genesis of silicosis the quartz acts as a " deposit poison " which slowly sets free the substances which determine a fibrogenic reaction. A similar opinion was put forward by King in saying that silica, in order to produce silicosis, must dissolve slowly enough to determine a prolonged reaction. These ideas agree with our opinion that the formation of fibrohyaline tissue which follows the action of quartz is dependent upon a slow but continued production of antigens.

It is now useful to consider hypothetically where the antibodies to these antigens might be produced. Some hints may be obtained from experimental immunology. A common method for obtaining an increased antibody response is that of introducing an antigen previously precipitated with $AlPO_4$, so that a granuloma forms, and it will be for a comparatively long time a source of concentrated antigen and a site of antibody production (White, Coons, and Connolly, 1955); it is interesting to note that the antigen-antibody precipitate which gradually takes place inside the granuloma has a strong tendency to be adsorbed by the collagen fibres which have been actively formed in the meantime.

Perhaps events might be similar in the silicotic granuloma which could therefore be at the same time a source of antigens and antibodies; the antigen-antibody precipitation would then begin in the central part of the nodule and the precipitate be absorbed by the reticular fibres with the formation of hyaline tissue as a result. In the meantime the proliferation of the peripheral cells could continue, thus increasing the size of the nodule. But it is possible that the antibody production is not limited to the cells of the silicotic granuloma. In the experiments of Coons *et al.* antibody production was not limited to the cells of the $AlPO_4$ granuloma but antibodies were produced to an even greater extent by cells in the regional lymph nodes. In silicosis the hilar lymph nodes might similarly be considered as a source of antibodies until they are totally invaded by the silicotic fibrosis, and in acute silicosis the hilar lymph nodes are swollen and very rich in cells (Di Biasi, 1949). Moreover, if the auto-antigens produced by the action of quartz were soluble, antibodies might be formed in other sites. Vigliani *et al.* (1950) have observed in silicosis an active proliferation of histiocytes and plasma cells in many extrapulmonary tissues, and a proliferation of reticular and plasma cells in the bone marrow of silicotics has been reported by Saita and Di Naro (1951) and by Lachnit (1954).

Conclusion

We consider that the immunological hypothesis of the pathogenesis of the hyaline tissue of silicosis and of progressive massive fibrosis is a working hypothesis which opens a new and promising field of research. It brings forward possible analogies between silicosis and some collagen diseases characterized by the presence of fibrinoid and amyloid substances, whose immunological origin appears increasingly probable.

The hypothesis is interesting in the emphasis it places on the rôle of the host organisms rather than on the action of silica. It is consistent, too, with a

number of the physical and chemical properties of silica but does not rely on them solely to explain the genesis of silicosis. Attention is focused more on the reaction of tissues and of the whole organism than on the toxic or irritating action of the foreign body. The hypothesis that this reaction is not confined to the mere cellular damage produced by silica but is concerned with the production of auto-antigens and auto-antibodies is in accord with some peculiarities which are common to silicosis and other diseases whose immunological genesis is very probable, that is, the formation of a hyaline substance chemically similar to amyloid, and the progressive course of the disease. Indeed, even when no more dust is inhaled, the formation of hyaline tissue goes on and leads to a massive fibrosis whose extension is much greater than that which might conceivably be produced by a purely toxic or surface action of the dust.

The immunological hypothesis outlined needs more precise verification, chiefly in regard to the possible mechanism of the formation of auto-antigens capable of inducing active production of auto-antibodies.

Summary

The histogenesis of silicotic nodules can be divided into two stages: first, cellular proliferation and the formation of reticular fibrils, and second, hyaline precipitation upon the fibrils. This second stage makes silicosis a disabling and progressive disease as compared with the uncomplicated pneumoconioses caused by inert dusts.

Our work on the origin of the hyaline stage of silicosis leads to the hypothesis that the hyaline tissue has an immunological origin and corresponds to an antigen-antibody precipitation. This opinion is supported by the following points:—

(1) The chemical composition of hyaline tissue of silicosis corresponds to that of amyloid, a substance for which an immunological origin is commonly accepted.

(2) Globulins have been demonstrated immunologically in silicotic nodules which were of the beta and gamma variety.

(3) Some aspects of silicosis, such as the increased gamma-globulin content of the blood, the proliferation of histiocytes and plasma cells in the reticuloendothelial system, the progressive course of the disease, and the variation in the reactions of individuals to inhaled silica dust, lead us to apply to silicosis the concept of " collagen disease ". Many of the collagen diseases have a recognized immunological origin.

(4) The influence of tuberculosis in producing massive hyaline fibrosis in silicotic patients can be explained on an immunological basis, assuming that the tubercle bacilli potentiate an antibody reaction, such as when Freund's adjuvant is used.

The possible mechanisms by which quartz could induce the formation of antigens capable of starting an antibody reaction are discussed.

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References

Antweiler, H., and Hirsch, E. (1956). *Arch. Gewerbepath. Gewerbehyg.*, **14**, 678.
Attygalle, D., Harrison, C. V., King, E. J., and Mohanty, G. P. (1954). *Brit. J. industr. Med.*, **11**, 245.
Boyd, W. C., and Bernard, H. (1937). *J. Immunol.*, **33**, 111.
Claeys, C. (1954). *Rev. méd. minière*, **7**, 22.
Cummins, S. L. (1940). *Brit. J. exp. Path.*, **21**, 64.
Dantin-Gallego, J. (1948). *Nuevas Ideas etio-patogenicas sobre la Silicosis.* Publicaciones de la Jefatura provincial de Sanidad, Madrid.
Di Biasi, W. (1949). *Beitr. Silikose-Forsch.*, No. 3.
Evans, S. M. (1948). *J. industr. Hyg.*, **30**, 353.
Freund, J., and McDermott, K. (1942). *Proc. Soc. exp. Biol. (N.Y.)*, **49**, 548.
Friedberg, K. F., and Lendle, L. (1956). *Beitr. Silikose-Forsch.*, No. 41, p. 1.
Grabar, P., and Williams, C. A., Jr. (1955). *Biophys. Biochim. Acta*, **17**, 67.
Gye, W. E., and Purdy, W. J. (1922). *Brit. J. exp. Path.*, **3**, 86.
Hale, L. W., Gough, J., King, E. J., and Nagelschmidt, G. (1956). *Brit. J. industr. Med.*, **13**, 251.
Holt, P. F., and Osborne, S. G. (1953). *Ibid.*, **10**, 152.
Holzapfel, L. (1952). *Beitr. Silicose-Forsch.*, No. 15.
Horsfall, F. L., and Goodner, K. (1936). *J. exp. Med.*, **64**, 583.
Jaffé, R. H. (1926). *Arch. Path. (Chicago)*, **1**, 25.
Jäger, R. (1954). In *Die Staublungenerkrankungen*, Vol. 2, p. 142, ed. Jötten, K. W., Klosterkötter, W., and Pfefferkorn, G., Steinkopff, Darmstadt.
Jones, R. S., and Frazier, D. B. (1950). *Arch. Path. (Chicago)*, **50**, 366.
Jötten, K. W., and Klosterkötter, W. (1952). *Arch. Hyg. (Berl.)*, **136**, 1.
Kikuth, W. (1956). *Dtsch. med. Wschr.*, **81**, 1633.
King, E. J. (1947). *Occup. Med.*, **4**, 26.
——, Harrison, C. V., Mohanty, G. P., and Nagelschmidt, G. (1955). *J. Path. Bact.*, **69**, 81.
——, Zaidi, S. H., and Nagelschmidt, G. (1956). *A.M.A. Arch. industr. Hlth*, **13**, 133.
Koch, W. (1949). *Frankfurt Z. Path.*, **60**, 58.
Koletsky, S., and Stecher, R. M. (1939). *Arch. Path. (Chicago)*, **27**, 267.
Lachnit, V. (1954). *Wien. Z. inn. Med.*, **35**, 49.
Letterer, E. (1949). *J. Path. Bact.*, **61**, 496.
——, Gerok, W., and Schneider, G. (1955). *Virchows Arch path. Anat.*, **327**, 327.
Parmeggiani, L. (1950). *Med. d. Lavoro*, **41**, 124.
Paterson, M. S., and Wheatley, K. H. (1955). Safety in Mines Research Establishment. Research Report No. 124.
Pernis, B. (1954). In *Die Staublungenerkrankungen*, Vol. 2, p. 293. Steinkopff, Darmstadt.
—— (1955). *Med. d. Lavoro*, **46**, 668.
——, and Clerici, E. (1957). *Ibid.*, **48**, 449.
——, and Ghislandi, E. (1956). *Ibid.*, **47**, 460.
——, Ceppellini, R., and Ghezzi, I. (1957). *Ibid.*, **48**, 380.
Policard, A., and Collet, A. (1954). *A.M.A. Arch. industr. Hyg.*, **9**, 389.
——, Croizier, L., and Martin, E. (1937). *Ann. Anat. path.*, **14**, 587.
Rüttner, J. R., Willy, W., and Baumann, A. (1954). *Schweiz. Z. Path. Bakt.*, **17**, 352.
Saita, G., and Arrigoni Martelli, E. (1956). *Med. d. Lavoro*, **47**, 367.
——, and Di Naro, C. (1951). *Ibid.*, **42**, 201.
Scheel, L. D., Smith, B., Van Riper, J., and Fleisher, E. (1954). *A.M.A. Arch. industr. Hyg.*, **9**, 29.
Seifert, H. (1954). In *Die Staublungenkrankungen*, Vol. 2, p. 199. Steinkopff, Darmstadt.
Teilum, G. (1948). *Amer. J. Path.*, **24**, 389.
Vazquez, J. J., and Dixon, F. J. (1956). *J. exp. Med.*, **104**, 727.
Velicogna, A. (1946). *Med. d. Lavoro*, **37**, 107.
Vigliani, E., Boselli, A., and Pecchiai, L. (1950). *Ibid.*, **41**, 33.
Vorwald, A. J. (1950). *Amer. Rev. Tuberc.*, **62**, Suppl. (July), p. 13.
Webster, I. (1956). *Leech*, **26**, 38.
White, R. G., Coons, A. H., and Connolly, J. M. (1955). *J. exp. Med.*, **102**, 73.
Williams, C. A., Jr., and Grabar, P. (1955). *J. Immunol.*, **74**, 397.
Zaidi, S. H., Harrison, C. V., King, E. J., and Mitchison, D. A. (1955). *Brit. J. exp. Path.*, **36**, 539, 545, 553.

Brit. J. industr. Med., 1958, **15**, 15.

TOXIC PROPERTIES OF SOME DIALKYL AND TRIALKYL TIN SALTS

BY

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Work reported in recent years from this laboratory has outlined the general features of poisoning in animals given di- and trialkyl tin salts (Stoner, Barnes, and Duff, 1955). More detailed accounts of the cerebral oedema produced by triethyl tin in rats (Magee, Stoner, and Barnes, 1957) and the bile duct and liver lesions produced by dibutyl tin salts in rats and mice have also been prepared (Magee and Barnes, 1957; Barnes and Magee, 1958).

A number of alkyl tin salts have been considered for industrial uses. The trialkyl salts are powerful fungicides (van der Kerk and Luijten, 1954) and also have an insecticidal action (Blum and Bower, 1957). The dialkyl tin salts, especially the dibutyl, have been employed as stabilizers in plastic tubing used for a wide variety of purposes. Dibutyl tin salts have also been used as anthelmintics for poultry (Kerr, 1952).

This paper summarizes observations made on 20 alkyl tin compounds given by several routes of administration to different species. Not every compound has been fully studied but data for general comparative purposes have been assembled and particular attention has been paid to those compounds likely to be used commercially.

The biochemical effects of these alkyl tin compounds are also being studied. Some observations have been published (Aldridge and Cremer, 1955; Cremer, 1957) together with a method of analysis (Aldridge and Cremer, 1957).

MATERIALS AND METHODS

Pure samples of all the tin compounds used in this work were supplied by Dr. van der Kerk, Organisch Chemisch Institut, T.N.O., Utrecht. In addition a supply of recrystallized dibutyl tin dichloride was given to us by Dr. Nancarrow of B.X. Plastics Ltd., and commercial preparations of some compounds were supplied by Pure Chemicals Ltd., and Albright and Wilson Ltd.

The animals used and general methods of administration of drugs are as described earlier (Stoner *et al.*, 1955; Magee, *et al.*, 1957). When Tween 80 or acetone was used as the solvent for intravenous injections the volume injected did not exceed 0·1 ml. per animal. The lethal doses and their 95% confidence limits were calculated by the method of Weil (1952).

RESULTS

Dialkyl Tin Salts

Dibutyl Tin Dichloride (D.B.T.C.).—The representative member of this group is dibutyl tin dichloride (D.B.T.C.) and its toxic effects will be described in some detail. Comparisons between other dibutyl tin salts and the dichlorides of other dialkyl tin compounds will be made.

Oral Toxicity in Rats.—A single dose of 50 mg./kg. D.B.T.C. in arachis oil made a rat ill for 24 to 48 hours after which recovery was usually rapid and complete. Accompanying the general toxic response there was a temporary dilatation of the stomach due to an accumulation of fluid and an inflammatory lesion of the bile ducts. The pathology of the bile duct lesion has been described elsewhere (Magee and Barnes, 1957; Barnes and Magee, 1958).

A single dose of 10 mg./kg. had no obvious effect but 20 mg./kg. produced a visible bile duct lesion. The dose response curve resulting from single doses of 50 to 400 mg./kg. by mouth was flat and it seems probable that much of the single large dose remained unabsorbed (Table 1).

TABLE 1

TOXICITY OF ORAL DIBUTYL TIN DICHLORIDE IN RATS

Dose (mg./kg.)	Number of Doses	Male	Female
50	1	0/4	0/4
50	3	5/6	0/6
50	3	4/12	4/12
100	1	0/4	0/4
100	3	5/6	6/6
200	1	1/4	1/4
200	3	6/6	5/6
400	1	4/4	2/4

The D.B.T.C. was given in solutions in arachis oil in multiple doses on successive days, and the mortality is recorded up to 10 days from the first dose expressed as deaths/number treated.

Successive daily doses of 50 mg./kg. had a more serious effect (Table 1) and the rats died either from the general toxic effect of the D.B.T.C. or, if they survived for seven days, died later from effects which were secondary to the damage to the bile ducts such as rupture of the duct with bile peritonitis or severe liver injury. The general toxic effects had no special feature. The animal sat quietly with staring coat and usually had some diarrhoea and was generally dirty in appearance. Those rats surviving doses of D.B.T.C. that produced severe bile duct damage with the death of 50% of the original group recovered completely and have been observed up to 15 months. At necropsy a permanently thickened and shortened bile duct was usually found but it appeared to have been functioning adequately.

Dibutyl tin dichloride has been fed to rats in their diet at levels of 20, 50, 75, and 100 p.p.m. for periods up to six months. The effects on growth and food intake are seen in Table 2. Rats on 20 p.p.m. grew normally and showed no lesions at necropsy. At 50 p.p.m. growth and food intake were usually reduced and seven out of 12 rats killed after six months had visible bile duct damage shown by thickening and dilatation of the duct and fibrosis of the pancreas. At 75 and 100 p.p.m. the rats showed a greater depression of growth than those on 50 p.p.m. There were deaths in each group on the higher level during the first four weeks but those surviving this period remained active and well. All survivors killed at six months showed some bile duct damage and this varied considerably in extent.

The administration of D.B.T.C. for these longer periods produced no pathological features that had not been seen in rats receiving single doses of D.B.T.C., and, although lighter in weight, the general condition of the animals was good even when necropsy revealed considerable biliary tract damage.

TABLE 2

EFFECT OF DIBUTYL TIN DICHLORIDE (D.B.T.C.) ADDED TO DIET OF GROWING MALE RATS

Concentration of D.B.T.C. in Diet (p.p.m.)	Experiment 1: 54 Days		Experiment 2: 55 Days	
	Weight (g.) Gain per Rat (mean ± S.D.)	Average Total Food Intake per Rat (g.)	Weight (g.) Gain per Rat (mean ± S.D.)	Average Total Food Intake per Rat (g.)
0	159 ± 9·7	723	172 ± 26·2	752
20	141 ± 22·7	712	—	—
50	129 ± 23·5^{++}	569	135 ± 34·8	577
75	—	—	112 ± 45·5^{+}	554
100	93 ± 10·4$^{\bullet}$	513	121 ± 44·2^{+}	609

$^{+}$ = significantly less than control mean at $P < 0.05$
$^{++}$ = significantly less than control mean at $P < 0.02$
$^{\bullet}$ = significantly less than control mean at $P < 0.01$

The D.B.T.C. was added to diet 41 powder as a solution in arachis oil. All groups contained six rats housed in one cage per group.

The acute effects of two other dibutyl tin salts—the dilaurate and the di-iso-octyl-thioglycollate—were compared with the dichloride by giving four daily doses of 50 mg./kg. to groups of four rats. No significant differences in response were observed.

Toxicity in Mice.—This species appeared slightly more susceptible to D.B.T.C. than the rat. Three daily doses of 50 mg./kg. killed nine of 12 mice and the survivors all had severe liver damage. Bile duct damage was also seen. At 20 mg./kg. bile duct and liver lesions were produced but the mice were not made seriously ill.

Toxicity in Rabbits.—Repeated daily doses of 25 and 50 mg./kg. led to the death of five out of eight rabbits within 10 days. No local lesion could be detected either in the biliary system or elsewhere to account for the death of the animals.

Toxicity in Guinea-pigs.—These animals withstood repeated daily doses of 50 to 100 mg./kg. D.B.T.C. and showed neither a general toxic reaction nor evidence of any biliary tract lesion.

Percutaneous Toxicity in Rats.—Successive daily applications of 10 mg. D.B.T.C./kg. over a period of 12 days produced a general loss of condition in rats as well as local skin damage with subcutaneous oedema and hyperaemia. Typical bile duct damage was found in these rats indicating that the dibutyl tin had been absorbed.

Rabbits showed more severe local damage in the skin from daily application of D.B.T.C. and their general loss of condition might have been the result of this injury alone. Guinea-pigs, on the other hand, were much more resistant and their skin showed little reaction to daily applications of 120 mg./kg. on five successive days.

Intraperitoneal Toxicity in Rats.—A dose of 7·5 mg. D.B.T.C./kg. injected into rats in 0·05 ml. of Tween 80 produced intense local irritation within the peritoneal cavity and death in a shock-like condition within a few hours. Tween 80 alone had no such action. The di-laurate had a similar effect indicating that it was the dibutyl tin and not the chloride that was responsible for the local lesion.

Intravenous Toxicity in Rats.—The full potentialities of D.B.T.C. as a toxic substance were studied by intravenous injections. The solvent was Tween 80. A dose of 5 mg. D.B.T.C./kg. produced visible bile duct injury within an hour of intravenous injection. As little as 2·5 mg./kg. produced bile duct injury that was discernible after 24 to 48 hours. These doses made the rat quiet for a few hours but it was not seriously ill. Ten mg./kg. resulted in death within 18 hours with an accompanying pulmonary congestion and oedema.

Rabbits and guinea-pigs were killed by doses of 5 to 10 mg./kg. They died 24 to 48 hours later with marked pulmonary congestion and oedema but no evidence of biliary tract injury.

Other Dialkyl Tin Salts Studied in Rats.—The toxicity of a number of other dialkyl tin dichlorides was studied and the results are summarized in Table 3 (intravenous), Table 4 (oral), and Table 5 (percutaneous). Particular attention was paid to the dioctyl tin salts when it was learnt that they would make effective substitutes for the more toxic dibutyl tin salts. To supplement the data in the Tables a few notes on each dialkyl tin dichloride compound tested follow:—

Dimethyl.—By intravenous injection this was the least toxic compound tested but on the skin it produced severe superficial damage in the rat and the guinea-pig. By mouth, large doses caused death with generalized weakness. No bile duct lesions were seen in rats.

Diethyl.—The toxic properties of these salts have been described earlier (Stoner *et al.*, 1955). Additional information from these experiments is that solutions applied to the skin produced a superficial necrosis accompanied by a more deep-seated inflammation. Damage to the bile ducts was noted

TABLE 3

THE INTRAVENOUS TOXICITY OF DIALKYL TIN DICHLORIDES MEASURED BY DEATHS IN RATS

Alkyl Group	Dose (mg./kg.)				Reactions	Bile Duct Lesions in Survivors
	5	10	20	40		
Methyl	–	0	0	2	No obvious cause of death No difference in toxicity of solution in Tween and acetone	None
Ethyl	–	0	1	4	Deaths 2-24 hr. after dose. No obvious cause	Slight
Propyl	0	3	4	–	Deaths usually within 12 hr. Some had pleural effusion	Moderate
*Iso*propyl	0	0	4	–	Death 2-72 hr. Loss of weight in survivors	Moderate
Butyl	0	4	4	–	Death 1-18 hr. Considerable lung damage	Severe
Pentyl	0	1	4	–	Death 1-18 hr. Pleural effusion often marked	Moderate
Hexyl	0	2	4	–	Death 2-4 hr.	Moderate
Octyl	0	4	4	–	Deaths usually within 4 hr. No gross lung damage	None
2. Ethyl hexyl	0	4	2*	–	Deaths 4-18 hr. No lesions	None
Trimethyl hexyl	0	4	2*	–	Deaths 4-18 hr. No lesions	None

* There were only two rats in these groups.

Intravenous injections of 0·05 ml. Tween 80 into female rats in groups of four.

TABLE 5

THE TOXICITY OF DIALKYL TIN DICHLORIDES APPLIED PERCUTANEOUSLY TO MALE RATS

Alkyl Group	Skin Lesion and General Reactions	Bile Duct Lesion
Methyl	Necroses of superficial layers of skin with black eschar formation. No deep-seated inflammation. Slight weight loss.	None
Ethyl	Slight superficial necrosis with patchy eschar. Generalized deep-seated oedema and subcutaneous inflammation.	None
Propyl	Lost weight and appeared generally ill. 2/3 died. White patchy necrosis of skin with deeper inflammation and oedema.	Slight
*Iso*propyl	Some weight loss. Not as ill as after propyl. Dry necrosis of skin. No eschar. Deeper oedema and inflammation.	Moderate
Butyl	1/3 died. Others less affected. Little superficial damage to skin but some oedema of subcutaneous tissues.	Marked
Pentyl	Rats became very irritable. No obvious skin lesions or subcutaneous oedema. Dark adrenals in one rat.	Slight
Hexyl	No loss of weight. No skin lesion.	None
Octyl	No loss of weight. No skin lesion.	None

The tin salts, 80 mg./kg., were dissolved in 0·1 ml. dimethylphthalate applied on five successive days to groups of three rats. Skin clipped. Rats observed for 12 days and at necropsy the skin lesion and condition of the bile duct were examined.

TABLE 4

THE COMPARATIVE ORAL TOXICITY OF DIALKYL TIN DICHLORIDES

Alkyl Group	40 mg./kg.	80 mg./kg.	160 mg./kg.
Methyl	No loss of weight. No bile duct lesion.	No loss of weight. No bile duct lesion.	Both died on fourth day with marked weakness. No bile duct lesion.
Ethyl	No loss of weight. No bile duct lesion.	One died. Lung congestion. One unaffected. No bile duct lesion.	Both died on fourth day. No lesions (see text).
Propyl	No loss of weight. No bile duct lesion.	One ill and killed fifth day. No lesion. One unaffected. No bile duct lesion.	One died second day. Pulmonary congestion. One lost weight. Recovered. Slight bile duct lesion.
*Iso*propyl	No loss of weight. Very slight bile duct lesion.	Slight loss of weight. Mild bile duct lesion.	Some loss of weight. Bile duct lesion.
Butyl	One died. Bile duct lesion. One lost weight.	Two died. One had severe liver lesion. Both had bile duct lesion.	Both very ill and lost weight. Severe bile duct lesions.
Pentyl	Both lost weight. Some bile duct damage.	One died fifth day. No necropsy. One lost weight. Adrenals red. Bile duct lesion.	Both lost weight. Adrenals very dark at necropsy. Slight bile duct lesion.
Hexyl	One lost weight and died. No bile duct lesion. One unaffected.	Both lost weight and then recovered. Adrenals very dark at necropsy. No bile duct lesion.	Both lost weight and one died. No bile duct lesion.
Octyl 2. ethyl hexyl	No loss of weight or bile duct lesion. 50 mg./kg. No ill effect.	No loss of weight or bile duct lesion. 100 mg./kg. No loss of weight or bile duct lesion.	One lost weight but no cause found. 200 mg./kg. No ill effect.

Oral doses were given to pairs of female rats on normal diet observed for 10 days from first dose; 40 mg./kg. given on first and fourth days, 80 mg./kg. on first and fourth days except di-hexyl given only on first day, 160 mg./kg. given on first day only except dibutyl and dioctyl given also on fourth day.

in all survivors of the intravenous toxicity test, and single oral doses of 200 mg./kg. produced typical damage to the bile ducts and dilatation of the stomach in 48 hours.

Di-n-propyl.—This was more toxic than the dimethyl or diethyl salt and after intravenous injection death was accompanied by pulmonary oedema. Percutaneously, it produced a generalized injury to the skin with deep-seated inflammation and oedema but less superficial necrosis than the dimethyl and diethyl salts. Bile duct lesions were produced.

Di-iso-propyl.—This salt was very similar to the di-n-propyl though bile duct lesions were more conspicuous after oral or percutaneous application.

Di-n-pentyl.—This salt was less toxic than the dibutyl by intravenous injection but also produced pulmonary oedema. It caused very little injury to the skin but bile duct lesions were seen after administration by all routes. In several rats dying after di-n-pentyl tin dichloride by mouth dark red adrenals were seen at necropsy. Microscopically the lesion was a haemorrhagic infiltration disrupting the gland. The lesion could not be consistently reproduced.

Di-n-hexyl.—Though more toxic by intravenous injection than the di-n-pentyl, the di-n-hexyl was less toxic by mouth or percutaneously. It produced bile duct lesions but only very slight injury to the skin. Again, adrenal damage was occasionally seen but could not be regularly produced.

Six rats given doses of 40 mg./kg. on four successive days by mouth all lost weight and one died. They continued to lose weight for 12 days but at necropsy no cause for this could be discovered.

Di-n-octyl.—Although as toxic as the dibutyl salt by intravenous injection the dioctyl salts were completely non-toxic by mouth or percutaneously. The cause of death in animals given intravenous doses was not clear. More extensive tests confirmed the non-toxicity of the dioctyl tin salts given by mouth to mice, guinea-pigs, and rabbits in doses up to 400 mg./kg. for three to four successive days. No ill effects of any kind were observed in any species. Groups of six young rats were given food containing 100 and 200 p.p.m. dioctyl tin dichloride for four months. They grew normally and were free from any lesions when killed.

Bis-2-ethyl hexyl (Di-iso-octyl) *Tri-methyl hexyl* (Di-iso-nonyl).—These salts had a similar intravenous toxicity to the di-n-octyl salts and were apparently completely non-toxic by mouth or applied to the skin.

Trialkyl Tin Salts

The members of this group of compounds that have been most extensively studied are the salts of triethyl tin and a detailed account of their toxic properties is given elsewhere (Stoner *et al.*, 1955; Magee *et al.*, 1957).

Triethyl tin acetate is soluble in water to the extent of about 3% and is equally toxic to rats by mouth or by intravenous injection (Table 6). The

TABLE 6

THE TOXICITY OF SINGLE DOSES OF TRIALKYL TIN ACETATE

Alkyl Group	LD50 (mg. Acetate per kg. Body Weight)	
Methyl (aqueous solution)	9·1	(7·0 – 11·8)
Ethyl	4·0	(2·9 – 5·5)
+Ethyl	4·2	(3·2 – 5·2)
++Ethyl	7·6	(6·4 – 9·0)
N-propyl	118·3	(98·3 – 142·4)
Iso-propyl	44·1	(36·1 – 53·9)
N-butyl	380·2	(238·1 – 607·3)
N-hexyl	1000*	
N-octyl	>1000**	

+ Intravenous route.
++ Male rats approximately 200 g. body weight.
* Two deaths in four rats given this dose.
** No deaths in four rats given this dose.

Except where otherwise shown the compounds were dissolved in arachis oil and given by mouth to female rats (approximately 200 g. body weight). The groups were kept for at least six and up to 21 weeks after administration and the LD50 calculated by Weil's (1952) method. The 95% confidence limits are shown in parentheses.

salient features of poisoning by a dose just exceeding the LD50 was an immediate period resembling mild anaesthesia lasting one to two hours followed by recovery. The rat, however, remained quiet and became progressively more ill with increasing muscular weakness and died within two to five days. The pathological lesion was oedema of the white matter of the central nervous system, but it is uncertain whether this alone accounted for the striking muscular weakness. A similar condition in rats may be produced by feeding a diet containing 10 to 20 p.p.m. triethyl tin hydroxide. Other species react somewhat differently to single doses. Rabbits show the initial mild anaesthesia and recover, but die within 24 hours after a series of convulsions of moderate severity. Hens tolerate its oral administration but are very sensitive to intravenous doses. Death may follow almost instantaneously or they recover completely after a few hours' unconsciousness.

The effects of other trialkyl tin salts on rats will now be briefly described. The LD50 for oral administration is given in Table 6. The reaction of rats to the intravenous injection of the higher homologues was very irregular in that some animals showed no reaction at all to a dose that was rapidly fatal to another rat of similar sex and age injected

immediately afterwards. For this reason an attempt to establish intravenous LD50s for each compound was not pursued. An effect apparently related to the different solvents—acetone and Tween 80—was noted in some cases. The solvent—water or acetone—did not influence the response of rats to triethyl tin acetate.

Trimethyl Tin Acetate.—As with the ethyl analogue the toxic dose by mouth was similar to that by intravenous injection. A characteristic picture was produced by either oral dosage or intravenous injection. There was an initial period of weakness with some degree of catatonia lasting several hours. After 24 hours generalized mild and continuous tremors developed with a pronounced irritability of the rats; a peculiar sparring among cage-mates might take place intermittently for two to three days. If the tremors were severe the animal would be prone in the cage with its tail held erect and its muscles in continuous tremor. Death might be delayed for up to eight days and some tremors might persist for the whole of that time. With very large oral doses (65 mg./kg. and above) there was generalized weakness and prostration as after triethyl tin.

Tri-n-propyl Tin Acetate.—A fatal oral dose produced death in two to four days and the rats had muscular weakness and an unsteady gait and were obviously ill. By intravenous injection the lethal dose was considerably less (24 mg./kg. killed seven out of eight rats). This always took place within 18 hours of the injection and was preceded by a progresive weakness of rapid onset. However, even the profound weakness seen in rats dying within 20 minutes was not accompanied by a true coma. Those surviving an intravenous injection for 24 hours had always recovered completely from any weakness they had displayed earlier.

Tri-iso-propyl Tin Acetate.—This was more toxic than tri-n-propyl tin both by mouth and by intravenous injection. A dose of 12 mg./kg. intravenously killed eight of 12 rats. They developed a weakness of sudden onset after intravenous injection which lasted up to four hours. At 3 mg./kg. recovery was complete within 24 hours. At higher doses there might be a sudden collapse and death within 10 minutes or a severe weakness only partly recovered from at 24 hours. By mouth the effects were of slower onset, and might last for up to eight days before the animal died. They walked unsteadily with a humped gait and general muscular weakness. Irritability was occasionally seen. A similar difference between the toxicities of tetra-*n*-propyl tin and tetra-*iso*- propyl tin has been reported by Caujolle, Lesbre, Meynier, and Blaizot (1955).

Tri-n-butyl Tin Acetate.—By intravenous injection this was more toxic than the tri-*iso*-propyl compound but death always took place within 10 minutes of the injection. Only an occasional rat of the 74 tested by this route of injection showed a persistent weakness such as was seen after tri-propyl tin salts.

By mouth tributyl tin acetate was much less toxic than the tri-propyl compounds and those receiving a fatal dose died within one to two days with the usual signs of weakness and a humped gait. In one group of four rats given 380 mg./kg., all became acutely ill and one died after 24 hours. The other three recovered and began to gain weight. After five weeks they again began to lose weight, became ill, and died six to seven weeks after injection. No cause of death could be established. In acute toxicity experiments on a series of tetra-alkyl tin compounds, Caujolle, Lesbre, and Meynier (1954a) emphasized the need for continuing such experiments for a considerable time in order to determine the full toxicity of the compound. In our experiments these were the only rats which died more than eight days after the administration of a single dose of any of the trialkyl tin compounds. Furthermore, these observations could not be repeated and rats survived larger doses of tributyl tin acetate without showing any such delayed effects.

Prolonged administration of tributyl tin was studied on three groups of 12 rats given 25, 50, and 100 p.p.m. tributyl tin acetate in their diet for three months. The growth curves are shown in Fig. 1. They showed slightly impaired health on feeding

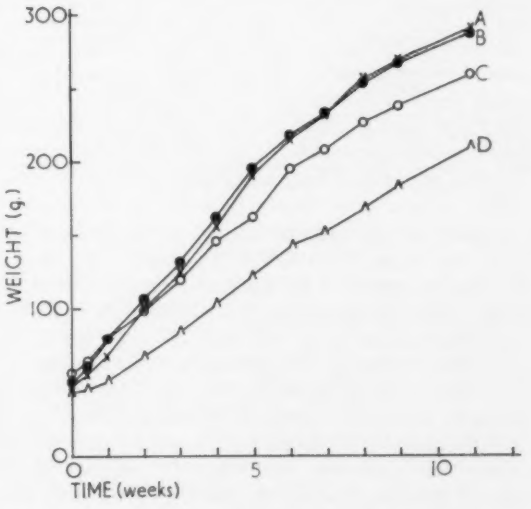

FIG. 1.—The growth curve of rats on diets containing tributyl tin acetate.
A = Control, B = 25 p.p.m., C = 50 p.p.m., D = 100 p.p.m.

50 p.p.m. and were more severely affected at 100 p.p.m. In this group two rats died during the first three weeks but the other animals recovered and were outwardly healthy when killed.

At necropsy four out of 11 rats on the highest level showed some degree of bile duct injury typical of dibutyl tin poisoning. No bile duct injury was seen in the other groups at the end of the experiment. The material used in the test was analysed and found to contain not more than 0·5% dibutyl tin. In view of these results, experiments are in hand to study the possible conversion of tributyl tin to dibutyl tin *in vivo*. The brain and spinal cord water content was also measured and at the highest level of intake the water content of the spinal cord was significantly increased (Table 7), but the increase was not large enough to be visible in histological sections.

To a single oral dose of tributyl tin acetate mice were as sensitive as rats. In the dose range 100 to 200 mg./kg. seven out of 32 died. All the animals were ill and lost weight for several days. The rabbits and the guinea-pigs were more sensitive and at a dose of 40 mg./kg. some animals died. They showed evidence of intense irritation of the alimentary tract, particularly of the caecum.

Solutions of tributyl tin acetate in alcohol or in arachis oil applied to the skin of rats, rabbits, and guinea-pigs caused a superficial encrustation but no deep-seated inflammation.

TABLE 7

EFFECT OF FEEDING TRIBUTYL TIN ACETATE IN DIET TO MALE RATS FOR 13 WEEKS ON PERCENTAGE WATER CONTENT OF BRAIN AND SPINAL CORD

Treatment	No. of Rats	% Water Content	
		Brain	Spinal Cord
Controls	5	78·2 ± 0·3	70·4 ± 0·5
25 p.p.m. tributyl tin acetate	5	77·8 ± 0·2	70·8 ± 1·6
50 p.p.m. tributyl tin acetate	5	78·0 ± 0·3	70·5 ± 0·7
100 p.p.m. tributyl tin acetate	5	78·7 ± 0·4	72·6 ± 1·0+

+ = significantly greater than control mean at $P < 0.01$.

Tri-hexyl Tin Acetate.—After intravenous injection of a lethal dose (6 to 12 mg./kg.) rats slowly became quieter and ruffled and after four to eight hours showed respiratory embarrassment and died with mild convulsions. At necropsy there was gross pulmonary oedema and pleural effusion similar to that seen in rats poisoned with α-naphthyl thiourea (Richter, 1946). No weakness or unsteadiness typical of poisoning by the lower homologues was noted in these rats. All four rats receiving 100 mg./kg. by mouth became ill and two died. This illness was of a more general type, again lacking the distinctive features of poisoning by the lower homologues. No naked-eye changes were seen at necropsy.

Trioctyl Tin Acetate.—This compound produced no effect at all in doses up to 48 mg./kg. intravenously or 1,000 mg./kg. by mouth.

PATHOLOGICAL FINDINGS

Naked-eye examination of rats dying after oral doses showed nothing abnormal. After intravenous injection moderate pulmonary congestion was sometimes seen in fatal poisoning by the tri-propyl and tri-butyl tin salts, but it was not enough to account for death. The pulmonary oedema and pleural effusion were almost certainly the cause of death after intravenous trihexyl tin salts.

The oedema of the white matter of the central nervous system produced by tri-ethyl tin salts has been described elsewhere (Magee *et al.*, 1957).

The estimation of brain and spinal cord water was carried out in rats dying after oral doses of certain other tri-alkyl tin salts and the results are given in Table 8.

TABLE 8

EFFECT OF TRIALKYL TIN COMPOUNDS ON WATER CONTENT OF BRAIN AND SPINAL CORD OF FEMALE RATS IN WEIGHT RANGE 190-205 g.

Compound	Oral Dose Acetate (mg./kg.)	Interval (days)	No. of Rats	% Water Content	
				Brain	Spinal Cord
(Controls)	—	—	6	77·2 ± 0·39	69·0 ± 0·39
Trimethyl	20	2	4	76·8 ± 0·26	69·4 ± 0·17
Trimethyl	30	2	3	77·0 ± 0·26	69·1 ± 0·89
Triethyl	8	2	5	79·1 ± 0·26++	74·1 ± 0·49++
Tri-*n*-propyl	200	3	4	78·8 ± 0·39++	72·0 ± 1·14++
Tri-*iso*-propyl	100	2	5	79·9 ± 0·82++	75·5 ± 1·77++
Tri-*n*-butyl	450	3	4	77·2 ± 0·48	68·1 ± 1·52
Tri-*n*-butyl	600	3	4	78·4 ± 0·69+	71·4 ± 1·62+
Tri-*n*-butyl	300	1			

++ = Significantly different from the controls at $P < 0.001$.
+ = Significantly different from the controls at $P < 0.01$.

Triethyl tin was the most active of these compounds and the activity of the higher homologues was of the same order as their toxicity. In spite of the profound effects produced by trimethyl tin salts on the central nervous system as judged by the behaviour of the animals, no oedema of the central nervous system was produced by trimethyl tin salts.

DISCUSSION

The lower dialkyl tin salts act upon biological systems *in vitro* in a similar manner to arsenicals (Aldridge and Cremer, 1955) and in neither case is the exact mechanism by which the poisoned animal is killed completely understood. This general toxic effect is counteracted in both cases by B.A.L.

Dimethyl and diethyl tin salts produce severe superficial injury to rodent skin but it is not known whether they would act as vesicants for human skin. Bile duct damage can be produced with the diethyl

but not the dimethyl tin salts but is more readily elicited by the higher homologues which produce a less striking injury to the skin. While lewisite (2-chlorovinyldichloroarsine) damages the biliary system of guinea-pigs but not of rats (Cameron, Carleton, and Short, 1946) the converse is true for the dialkyl tin salts.

Hitherto the chief industrial interest has been in the dibutyl tin salts which have been added to certain plastics as stabilizers. There are no published data to indicate whether or not these compounds would leach out of a finished plastic tube or wrapping into the liquid or food in contact with such material. From our study of the effects of dibutyl tin dichloride in the diet the highest harmless level for the rat appears to be about 20 p.p.m. Using the conventional 100-fold safety factor a safe level in food should certainly not exceed 0·2 p.p.m. Extrapolation of data from rats to man in this case is particularly difficult because it is known that the guinea-pig and hen are much less susceptible to the toxic action of dialkyl tin salts by mouth while the mouse is possibly rather more susceptible than the rat. Although it is difficult to draw definite conclusions from the French cases of alkyl tin poisoning (see below), they do show that man is affected by these compounds.

The problem of toxic residues of dialkyl tin stabilizers used in plastics which may come into contact with food may be resolved if the dioctyl or a similar higher analogue is used. These have no demonstrable toxicity to rats, rabbits, or guinea-pigs when given by mouth or applied to the skin in large doses nor do they have any action on the biochemical systems studied *in vitro* (W. N. Aldridge, personal communication).

The trialkyl tin compounds have been studied in considerable detail because their mode of action appears to be distinct from that of other well-known metabolic poisons. In high dilution *in vitro* they inhibit oxidative phosphorylation by mitochondria (Aldridge and Cremer, 1955). Similarly, when slices are prepared from triethyl-tin-treated rats only the O_2 uptake of the brain slices is impaired although most of the triethyl tin is concentrated in the liver and erythrocytes. In the whole animal the pharmacological and pathological effects are practically confined to the nervous system (Stoner, *et al.*, 1955; Magee, *et al.*, 1957), but alterations in the metabolism of phosphate compounds can be demonstrated both there and in the liver (Stoner and Threlfall, 1958). The observations made so far seem to indicate a failure in the utilization of chemical energy rather than a disturbance in its production in mammals poisoned by triethyl tin, but the mode of action of the trialkyl tin compounds is not known.

From the practical point of view it is important to remember that the action of triethyl tin upon the central nervous system is reversible in the rat (Magee, *et al.*, 1957). No permanent brain cell damage or tract demyelination is produced as in the case of the alkyl mercury derivatives (Hunter, Bomford, and Russell, 1940). This may be an important point to bear in mind when comparing the possible hazards in handling the two groups of compounds as fungicides.

Triethyl tin has a good fungicidal activity and is also very toxic to animals. Tributyl tin appears to be an equally good fungicide (van der Kerk and Luijten, 1954) but is much less toxic to rats. Fed to rats over a period of three months tributyl tin acetate produced no symptoms at a level of 50 p.p.m. in the food though at 100 p.p.m. some oedema of the central nervous system was produced. Studies *in vitro* demonstrate little difference in the power of triethyl and tributyl tin to inhibit oxidative phosphorylation (W. N. Aldridge, personal communication). This may explain why both have fungicidal activity. The lesser toxicity of the tributyl tin salts cannot yet be explained but may be due to differences in the rate of absorption and ultimate distribution in the body. Preliminary observations point to species differences in the sensitivity to these salts given by mouth. The higher homologues such as trioctyl tin acetate are inactive as fungicides and without toxic effect on the whole animal or those mammalian biochemical preparations which have been studied *in vitro*.

Up to the present the only reports of human poisoning from alkyl tin compounds have come from France where a preparation alleged to be diethyl tin diiodide was widely sold for a time as a treatment for skin diseases. Although there were many fatalities and many non-fatal cases there have been no reports of long-term disabilities such as occur after poisoning by alkyl mercury derivatives. Even severe cases of poisoning do not appear to have been necessarily fatal (Rouzaud and Lutier, 1954). Although the main tin ingredient of the preparation was in the dialkyl form the main feature of the poisoned cases was cerebral oedema which in animals is characteristic of poisoning by trialkyl tin. This might indicate that trialkyl tin was present as an impurity, in which case it would seem that man is very sensitive to the action of this form of tin. The hazards that might accompany the use of trialkyl tin compounds as fungicides in agriculture cannot be accurately gauged. While B.A.L. would probably be an effective remedy for poisoning by dialkyl tin compounds no rational therapy can yet be suggested for poisoning by trialkyl tin salts.

From the toxicological point of view the tetra-

alkyl tin compounds can be considered to behave in an analogous way to their trialkyl counterparts (Jolyet and Cahours, 1869; Lecoq, 1954; Stoner, *et al.*, 1955; Caujolle, *et al.*, 1955; Caujolle, *et al.*, 1954a, b). This may be explained by their conversion to the trialkyl derivatives in the body as this has recently been demonstrated for tetraethyl tin *in vitro* by Cremer working in this laboratory.

SUMMARY

The toxicity of a series of di- and trialkyl tin compounds has been studied after their administration by different routes in a number of species.

There is a striking difference in the response to the two groups of compounds. The dialkyl tin compounds cause a generalized illness with damage to the biliary tract as the main pathological feature. The trialkyl compounds act on the central nervous system where the majority of them produce an interstitial oedema.

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REFERENCES

Aldridge, W. N., and Cremer, J. E. (1955). *Biochem. J.*, **61**, 406.
——, ——, (1957). *Analyst*, **82**, 37.
Barnes, J. M., and Magee, P. N. (1958). *J. Path. Bact.* In press.
Blum, M. S., and Bower, F. A. (1957). *J. econ. Ent.*, **50**, 84.
Cameron, G. R., Carleton, H. M., and Short, R. H. D. (1946). *J. Path. Bact.*, **58**, 411.
Caujolle, F., Lesbre, M., and Meynier, D. (1954a). *C.R. Acad. Sci. (Paris)*, **239**, 1091.
——, ——, —— (1954b). *Ibid.*, **239**, 556.
——, ——, ——, and Blaizot, A. (1955). *Ibid.*, **240**, 1732.
Cremer, J. E. (1957). *Biochem. J.*, **67**, 87.
Hunter, D., Bomford, R. R., and Russell, D. S. (1940). *Quart. J. Med., n.s.*, **9**, 193.
Jolyet, F., and Cahours, A. (1869). *C.R. Acad. Sci. (Paris)*, **68**, 1276.
Kerk, G. J. M. van der, and Luijten, J. G. A. (1954). *J. appl. Chem.*, **4**, 314.
Kerr, K. B. (1952). *Poult. Sci.*, **31**, 328.
Lecoq, R. (1954). *C.R. Acad. Sci. (Paris)*, **239**, 678.
Magee, P. N., and Barnes, J. M. (1957). *Ned. T. Geneesk.* In press.
——, Stoner, H. B., and Barnes, J. M. (1957). *J. Path. Bact.*, **73**, 107.
Richter, C. P. (1946). *Proc. Soc. exp. Biol. (N.Y.)*, **63**, 364.
Rouzaud, M., and Lutier, J. (1954). *Presse méd.*, **62**, 1075.
Stoner, H. B., Barnes, J. M., and Duff, J. I. (1955). *Brit. J. Pharmacol.* **10**, 16.
——, and Threlfall, C. J. (1958). In preparation.
Weil, C. S. (1952). *Biometrics.*, **8**, 249.

THE OCTOBER (1957) ISSUE

The October (1957) issue contains the following papers:—

Experimental Studies on the Relative Importance of Concentration and Duration of Exposure to Dust Inhalation. By B. M. Wright.

The Effect of the Use of Calcined Alumina in China Biscuit Placing on the Health of the Workman. By A. Meiklejohn and E. Posner.

Air Pollution in Diesel Bus Garages. By B. T. Commins, R. E. Waller, and P. J. Lawther.

Observations on Urinary Cadmium and Protein Excretion in Men Exposed to Cadmium Oxide Dust and Fume. By J. C. Smith and J. E. Kench.

Chemical and Histological Post-mortem Studies on a Workman Exposed for Many Years to Cadmium Oxide Fume. By J. C. Smith, J. E. Kench, and J. P. Smith.

An Investigation into the Acute Respiratory Reaction to the Inhalation of Tamarind Seed Preparations. By Peter G. Tuffnell and I. Dingwall-Fordyce.

A Review of 102 Cases of Beat Conditions of the Knee. By W. B. Roantree.

Ventilation of Impermeable Clothing. By G. S. Christie, J. P. Gleeson, W. G. Jowett, and A. S. Wright.

Absence and the Physical Conditions of Work. By R. D. Shepherd and J. Walker.

Azo Dyes and Heinz Bodies. By Philip Rofe.

Experience of Pulheems in the 1952 Army Intake. By S. Rosenbaum.

The Efficiency of Various Liquid Impinger Samplers in Bacterial Aerosols. By K. R. May and G. J. Harper.

Miscellanea:

The Range of Vision Permitted by Protective Goggles. By J. P. Bull.

Book Review.

Index.

A number of copies are still available and may be obtained from the Publishing Manager, British Medical Association, Tavistock Square, W.C.1, price 12s. 6d.

Brit. J. industr. Med., 1958, **15**, 23.

PULMONARY DISEASE AMONGST SISAL WORKERS

BY

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(RECEIVED FOR PUBLICATION JUNE 11, 1957)

The sisal industry is economically one of the most important in Kenya as it employs about 8,000 Africans who are engaged on work in 69 sisal plantations in the Colony. This corresponds to about 2% of the total number of Africans employed in all public services, agricultural, and other industries.

Employees on sisal estates are broadly speaking subject to the same diseases as other agricultural workers except that possibly tropical ulceration of the leg is more prevalent amongst them. The dusty conditions created by the brushing machines in the sisal factories, may, however, cause special hazards, as, apart from the general nuisance value of the dust, and its irritative action on the eyes and the upper respiratory tract, there remains the possibility that it might be responsible for damage to the lung tissue.

The only reference in the literature which can be found which deals with the effect of sisal dust on the pulmonary tissues is that of an investigation carried out recently by Martins (1956) who clinically examined 118 operatives employed in the brushing rooms of three sisal estate factories in Mozambique. He reported that respiratory incapacity was more prevalent amongst brushing-room workers than others, and that he could find no " flagrant signs of pneumoconiosis " ; but it should be pointed out that he had no radiological facilities.

Although this report by Martins is the only one available on sisal dust it is well known that other organic dusts of vegetable origin are capable of causing lung damage. Broadly speaking these dusts may affect the lungs in three different ways. First, they may produce allergic, asthmatic, and bronchitic conditions. A classical example is byssinosis, first described by Leach in 1863, and contracted by a considerable proportion of operatives working in the card- or blow-rooms in cotton mills. Asthmatic or bronchitic attacks may also occur amongst workers in the woollen industry (Moll, 1933), and amongst bakers (Anton, 1934; Ordman, 1947) and millers (Linko, 1947).

Secondly, pulmonary disease may be caused by the inhalation of organic dust containing bacteria, fungi and moulds, and in particular, pulmonary mycosis may occur amongst persons exposed to moulded grain or hay (Fawcitt, 1936; Törnell, 1946; Hoffmann, 1946). A variety of fungi may be the causative agents, but *M. albicans*, *M. candida*, and *A. fumigatus* appear to be the most frequent. Other fungi may also cause an allergic state giving rise to asthma and vasomotor rhinitis, and mites contaminating grain have been reported to give rise to pulmonary symptoms (Marcandier and Le Chuiton, 1928; Najera Angulo and Dantin Gallego, 1939). Caminita, Baum, Neal, and Schneiter (1947) have incriminated *Aerobacter cloacae* as being responsible for " mill fever " in cotton operatives. Schilling (1956) has described the same condition in workers preparing hemp and flax for spinning.

A third possibility of pulmonary damage arising from exposure to vegetable dusts may be due, not to the effect of the dust itself, but to a high content of free silica mixed with it. Thus the pulmonary fibrosis in workers occupied in the stemming and redrying of tobacco from North Carolina is not due to the tobacco dust itself but to its admixture with free silica which occurs in high content in the soil in which the tobacco is grown (McCormick, Smith, and Marsh, 1948).

Finally there is a group of pulmonary affections caused by organic dusts the aetiology of which are in doubt. One such disease is bagassosis which was first described by Jamison and Hopkins in 1941, and which results from exposure to the dust of the fibre trash remaining after the extraction of sugar from the sugar cane. Dunner, Hermon, and Bagnall (1946) have reported radiological findings of reticulation, mottling, and fibrosis amongst dockers handling grain and seeds, and they concluded that mycotic organisms were unlikely to have caused these changes.

Scope of the Present Investigation

The present investigation was designed to deter-

mine whether sisal dust could cause pulmonary lesions and incapacity amongst workers exposed to it. A factory was chosen where the dust problem was apparently bad, the labour turnover was relatively small, the labour records were good, and the management cooperative. It manufactured "gunny" bags and rope from sisal, and was the only one of its kind in Kenya. In general the dust conditions in the carding room of this factory were similar to the dustiest brushing rooms of sisal estate factories elsewhere.

The investigation was started in January, 1955, but in the previous November an additional new factory had been opened on the premises for the purpose of manufacturing bags from jute. The present investigation centred on the old factory which was exclusively concerned with processing sisal.

Conditions in the Factory

A total of 1,314 Africans were employed, 1,038 of whom worked in the old factory. The great majority of the employees were men, but it had recently become the policy to employ more of the wives and female relatives of the male staff.

Fig. 1 shows the layout of the different departments of the old factory. The generation of dust was almost entirely confined to the batching and carding departments which can be seen at the bottom of the plan. A small amount of sisal dust was also produced from one machine in the rope plant, but otherwise airborne dust was virtually non-existent. The carding room was partially separated from the adjoining departments in the factory by a hessian screen which was hung from the ceiling to within about seven or eight feet of the floor. At the time the investigation was undertaken there was no artificial means of ventilation, but an extraction plant has since been installed with most satisfactory results.

The manufacturing process was started in the batching and carding rooms where sisal tow was passed through teazer cards in which the entangled lumps of short fibres were torn apart, and extraneous matter was removed from the tow. The fibre was delivered from these cards in the form of a fleece which was then hand sprayed with an oil-and-water emulsion. After this it was allowed to stand for several hours to allow the emulsion to permeate the bundles thoroughly. This was the batching process, and the purpose of spraying with oil was not to keep the dust down but to render the sisal fibres more pliable. The batched fleece was then broken down by a series of teethed rollers in a breaker card and emerged in a broad sliver. The sliver then passed through a finishing card, which operated in the same way as the breaker card, but which produced a more refined and cleaner ribbon.

The sliver then left the carding room, and went through a series of processes none of which generated any dust. It was first refined in drawing machines by being drawn out and levelled on rollers; it then passed to the spinning department where it was converted into yarn by the action of flyers, and wound on bobbins. The bobbins of the weft and warp yarn were then rewound on the cop and spool machines respectively. A coat of sizing containing hot maize flour paste was applied to the warp which was then carried over heated drums in a dressing machine. The weaving was carried out on a Dundee hessian loom, and the woven cloth from the looms was taken to the finishing department where it was first passed through the four heavy rollers of a calendering machine, and then through a mangle which gave the finish to the cloth by ironing it out. Finally the sisal cloth was passed to the sewing department where it was cut into suitable lengths and made into bags by special sewing and hemming machines.

The factory operated four shifts. Three of them, each of eight hours, covered the 24 hours. The fourth was an extra shift worked daily between 6 a.m. and 2 p.m. The work in the factory was stopped at 6 a.m. on Sunday morning and restarted at the same time on Monday morning.

Sickness Rates in the Old Factory.—The firm operated two dispensaries; one was situated in the old factory block, and one in the labour lines. They were staffed by ex-army dressers who had gained a rudimentary medical knowledge in the army, and who were able to make simple diagnoses which were almost entirely referred to symptomatology. Thus the sick register contained such diagnoses as "cough", "chest pain", "diarrhoea", and "vomiting". The purpose of the dispensary in the factory was to provide first-aid treatment for the employees themselves either for medical or surgical conditions. The dispensary in the labour lines provided similar treatment for the families, and for those workers who wished to consult a dresser in their off time.

An analysis of all medical cases seen by one of the dressers in the factory dispensary over a period of four months was made from the register. All medical conditions diagnosed were classified into two groups. In the first group were classed all complaints referring to respiratory and chest conditions, whilst all other medical complaints were classed in the second group. A further subdivision of these groups was made by determining whether the patient was working in the dusty carding room or

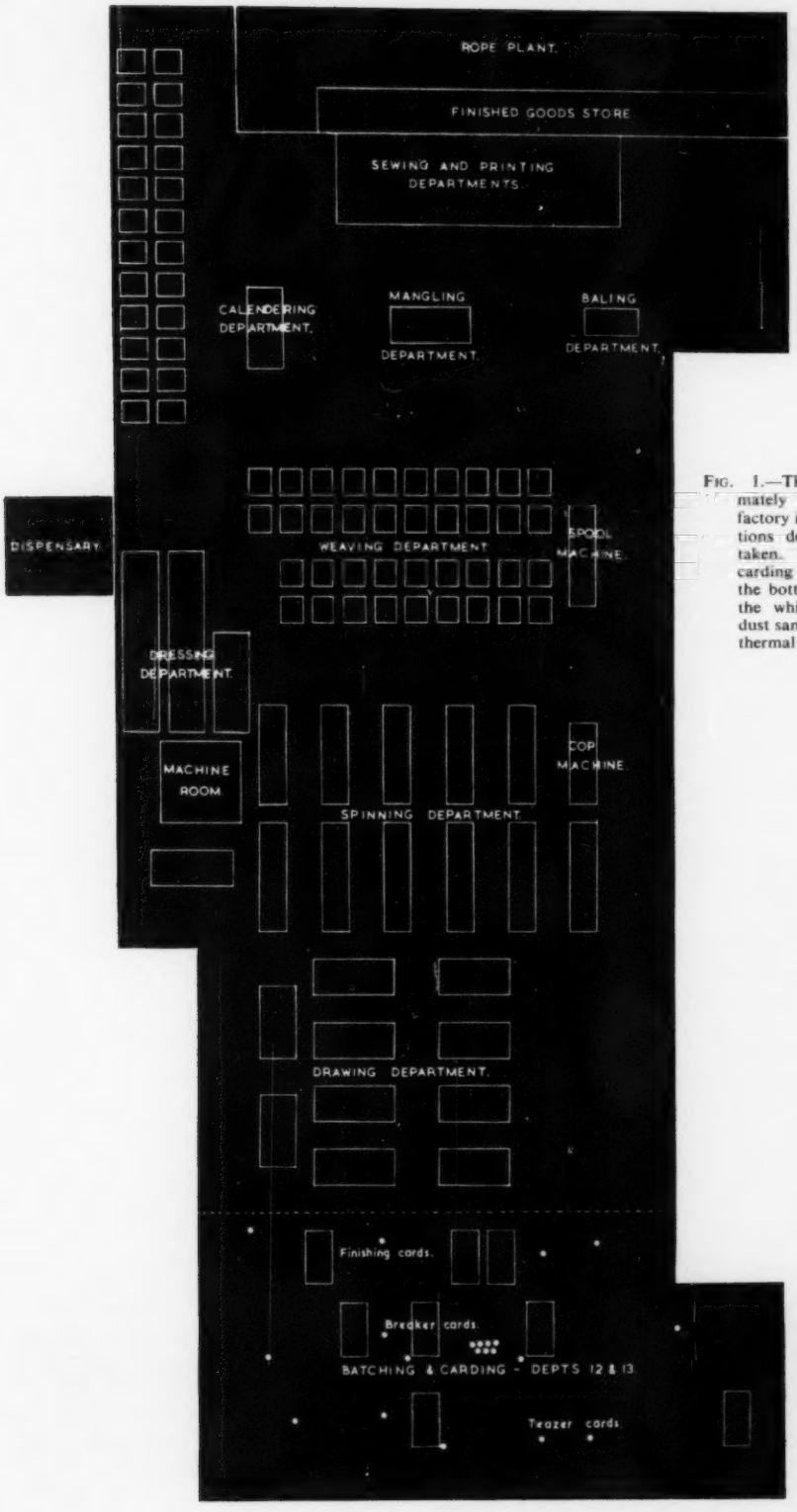

FIG. 1.—The layout (approximately to scale) of the old factory in which the investigations described were undertaken. The batching and carding department is seen at the bottom of the chart, and the white dots indicate the dust sampling positions of the thermal precipitator.

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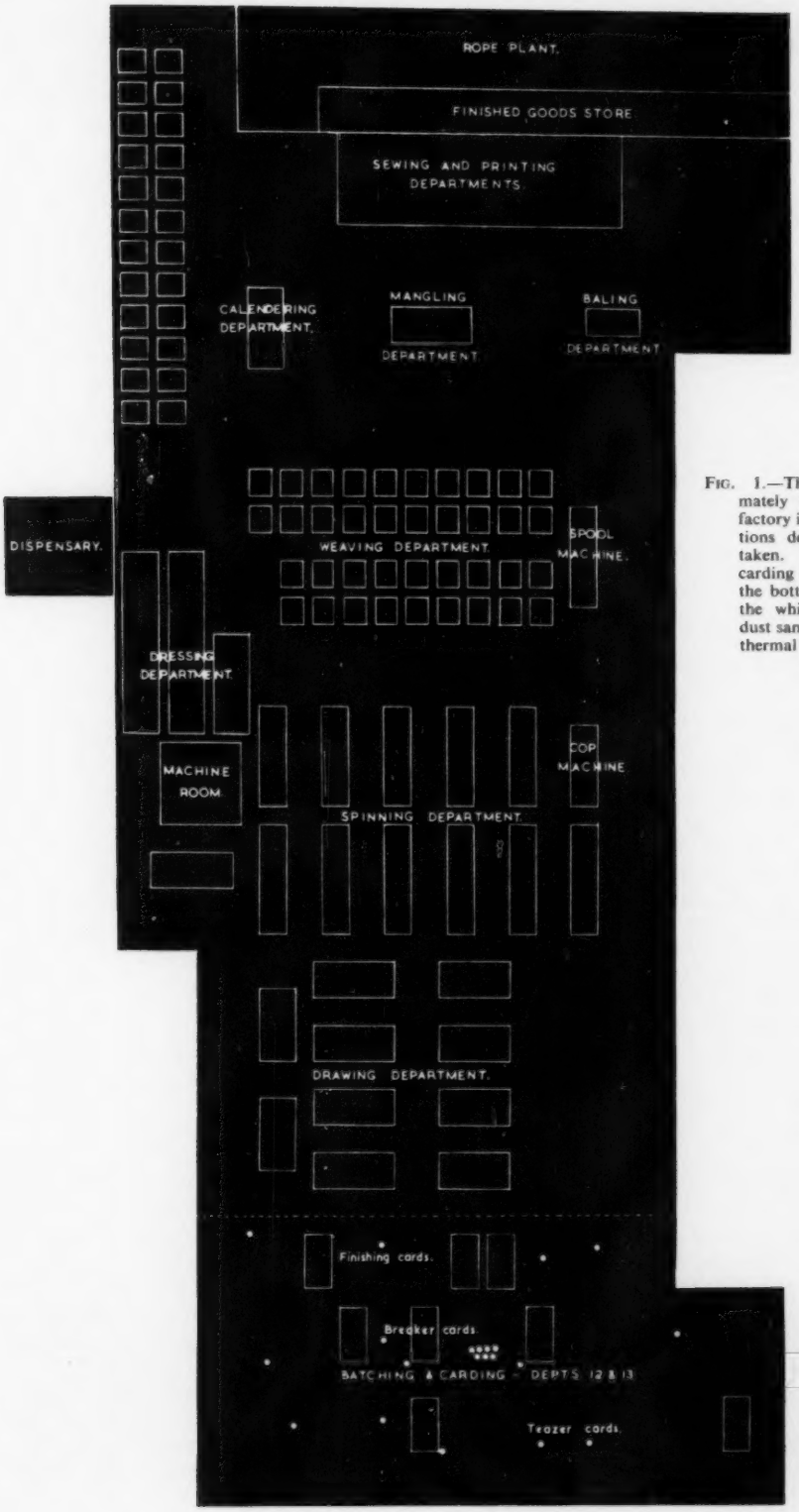

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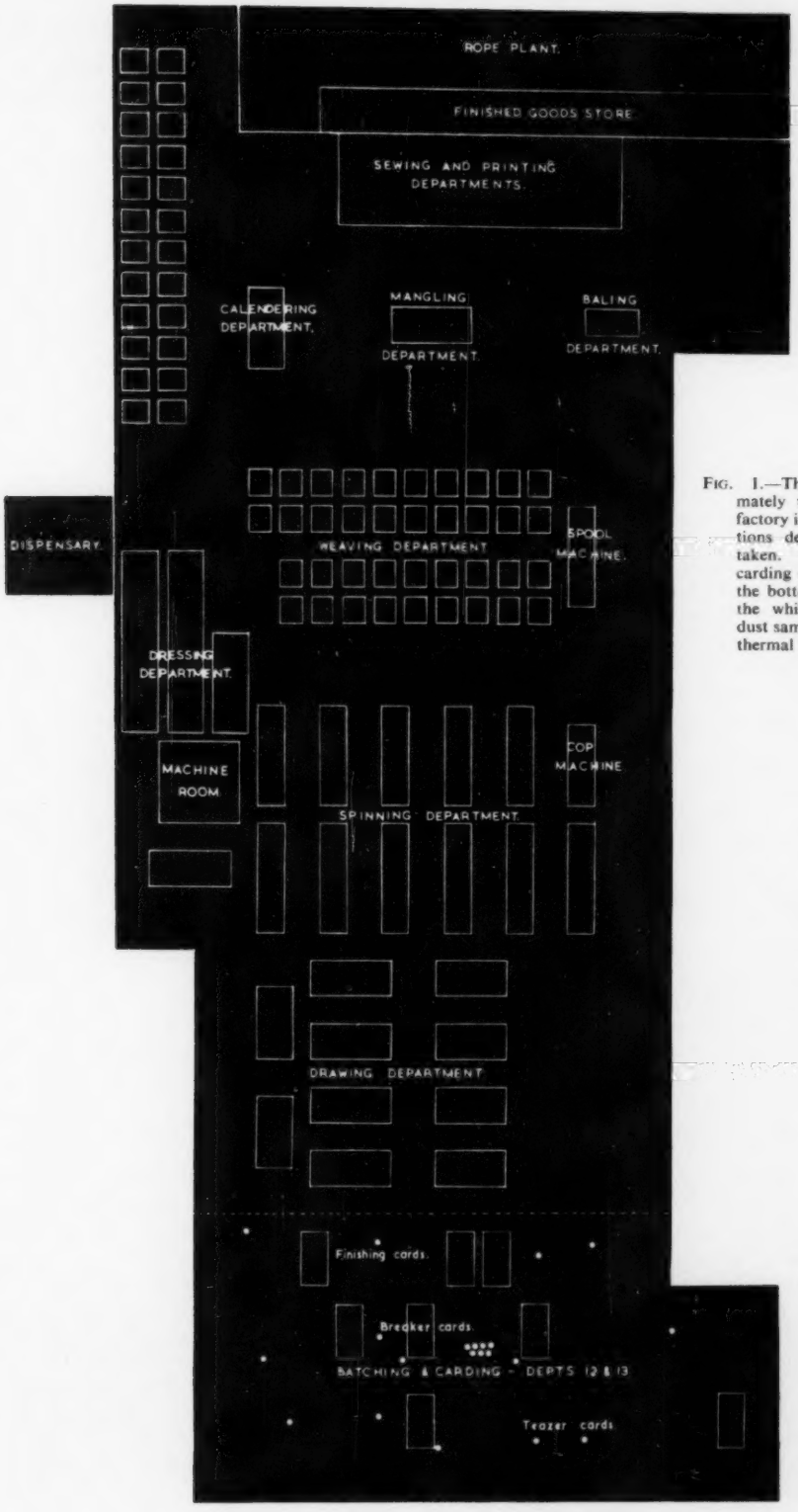

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in other departments where there was no dust when he developed his symptoms. Owing to the absence of any record of the ages of the workers it was impossible to compare their relative age structure, but from general observation of those at work in the different departments no great difference was observed in the ages of those working in the carding room and those working in other departments.

TABLE 1

PERCENTAGE OF ATTENDANCES OF ALL EMPLOYEES ON ACCOUNT OF CHEST COMPLAINTS IN WORKERS IN CARDING ROOM AND IN OTHER DEPARTMENTS

	Average Total Persons Employed	Total Attendances	%Attendances of Total Employed
Carding room	130	70	53·8
Other departments	908	232	25·6

Table 1 shows that the attendance rate for chest conditions was twice as high in workers in the carding room as in other departments. It will be observed that both sets of figures are abnormally high when compared with similar figures in other parts of the world, but the partiality of the African for taking medicine for the most trifling complaints is undoubtedly one cause. However, this high total rate should not affect the comparison between the two groups of workers in the same factory.

The exact nature of the respiratory infections contracted is again uncertain but it is probable that the majority of chest conditions were acute infections of the upper respiratory tract. Particular attention was paid to questioning the dresser, and also some of the long-term employees in the carding room. The dresser in seven years' experience could only remember seeing one case of asthma in a worker from the carding room, and all other persons questioned denied that they recognized chest tightness or respiratory upset of any kind occurring typically on a Monday morning or after a period away from work. It is considered improbable therefore that symptoms similar to those in byssinosis are caused amongst Africans as the result of inhalation of sisal dust.

A search of the medical records in the factory showed that since 1950 there had been 74 men with acute chest conditions who had been treated in hospital. In 48 of these cases it was possible to identify the department in the factory in which the man was actually working when he contracted the disease. It was noted that whereas carding room workers comprised about one-quarter (11 out of 48) of those admitted to hospital they represented only about one-eighth (130 out of 1,038) of the total factory population.

An attempt was then made to trace the hospital records of these 48 persons with a view to discovering the type of chest condition from which they suffered. Unfortunately many of the records had been destroyed, and it was only possible to obtain the bed head tickets of 24 of the cases. In three cases a diagnosis of acute bronchitis had been made, and there was nothing to indicate that the disease was anything more; none of these persons had ever worked in the carding room. In the other 21 cases a diagnosis of lobar pneumonia had been made, and an examination of the case histories confirmed that the disease was in every case almost certainly lobar pneumonia. Its predominating features were sudden onset of cough, chest pain, and pyrexia, with rusty sputum in many cases, unilateral chest signs, quick response to sulphonamides or penicillin, and rapid convalescence. Four of these persons had developed the disease while working in the carding department, and its course appeared to be as typical of pneumonia as in any of the others. No case had been radiographed while in hospital, but it was possible to radiograph 10 of those workers who had previously suffered from lobar pneumonia, and three of whom had developed the disease while working in the carding room. No abnormalities were seen in the lung fields of any of these patients, but four of them showed evidence of pleural or diaphragmatic adhesions, and two of these had been carding room workers. There was therefore some evidence to indicate that lobar pneumonia was commoner amongst workers exposed to sisal dust than amongst those not exposed to it.

It should be noted that Martins in his survey of sisal brushing room operatives also found that respiratory infections were commoner amongst these workers, but in contradistinction to the present investigation he found that asthma occurred more frequently in those exposed to sisal dust than in others. He gives the incidence of asthma in brushing room operatives as 1·6% against an incidence of 0·1% in other general workers.

Nature of the Carding Room Dust.—The atmosphere in the carding room was thick with dust, and it was obvious that the main concentrations lay around the carding machines, particularly the teazer cards, and in the batching area. The daily variation in the amount of dust produced was not marked. The operatives working in the room were invariably covered with a film of grey dust; some wore cloth masks over their mouths but the great majority wore nothing. To an unacclimatized visitor the dust had a mildly irritant effect on the upper respiratory passages, and caused some irritation to the eyes.

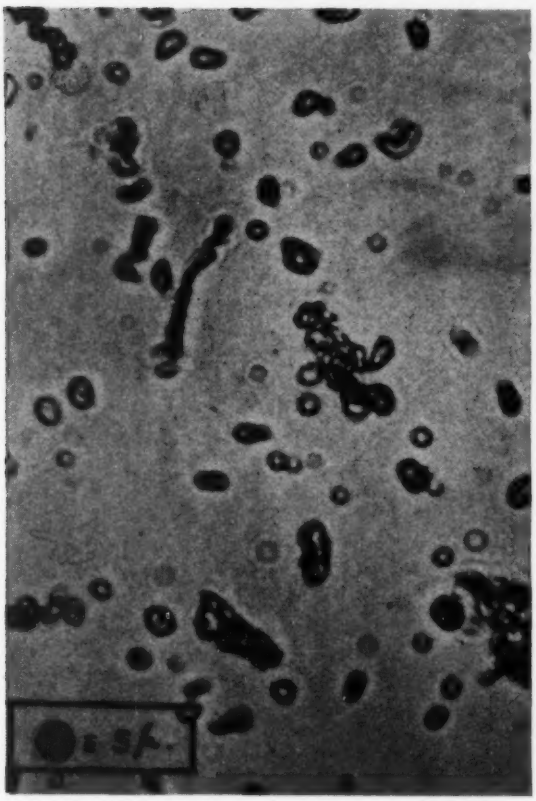

FIG. 2.—Photomicrograph of sisal dust collected by the thermal precipitator.

Dust Sampling by Thermal Precipitator.—Twenty-one samples of the dust in the carding room were collected with the thermal precipitator. The samples, which were taken at breathing level, were collected on different days and from different positions in the room. All sampling positions are indicated in Fig. 1. No dust counts were performed in other departments of the factory as it was obvious that dust concentration in these was minimal. A total and differential dust count was performed on each sample. An average of 1,000 particles were counted for each total count, and 500 for each differential count. A photomicrograph of a sample of the dust collected is shown in Fig. 2. The results of the counts are given in Table 2, and the estimated dust count in the room, as judged from the average of all 21 samples taken is shown. The average dust concentration in the neighbourhood of the carding machines, and also at the periphery of the room, have been calculated separately.

The concentration of dust in the neighbourhood of the carding machines was found to be over twice as great as it was round the periphery of the room. The highest dust count which was recorded was 1,787 particles (0·5-5μ range) per ml.; this sample was taken from near a teazer card. The lowest count was 30 particles (0·5-5μ) per ml. and this sample was taken from the periphery of the room. As most of the work in the carding room was performed in the immediate vicinity of the machines the workers were exposed for most of their time to the heavier rather than lower concentrations of dust. A further factor of some importance has to be considered. The addition of an oil-and-water emulsion to the sisal fleece in the batching process was said by the staff in the factory to have had a very noticeable effect in diminishing the amount of dust in the atmosphere. This procedure had only recently been introduced whereas previously it had been the custom to moisten the fibre with water only when necessary. For this reason it is probable that the concentrations of dust had previously been higher in the carding room than they were found to be at the time the present investigations were undertaken.

TABLE 2

AVERAGE CONCENTRATION AND SIZE DISTRIBUTION OF DUST FROM 21 SAMPLES TAKEN FROM DIFFERENT POSITIONS IN CARDING ROOM

	Proximal to Carding Machines (14 samples)	Distal to Carding Machines (7 samples)	Average in Carding Room (21 samples)
Total count (particles per ml. 0·5-5μ range)	302	124	243
Differential count (% in each size group) :			
Over 5·0 microns	5·0	4·8	4·9
5·0 ,,	2·4	2·1	2·3
4·0 ,,	3·6	2·8	3·3
3·0 ,,	4·6	3·8	4·3
2·5 ,,	5·0	4·1	4·7
2·0 ,,	5·6	4·7	5·3
1·6 ,,	8·0	7·5	7·8
1·2 ,,	11·2	8·3	10·2
0·8 ,,	17·2	14·6	16·4
0·4 ,,	19·3	22·5	20·5
0·2 ,,	18·1	24·8	20·3
Median size (microns)	0·72	0·56	0·66

After the installation of the dust extraction plant in the carding room the reduction of the dust in this room was most noticeable visually. Two dust samples were taken from a sampling position in the middle of the room between two breaker cards, and from which seven samples had been taken before the installation of the plant. (The position can be identified in Fig. 1.) The average count of particles, between 0·5 and 5μ, of the two samples taken after the installation of the extraction plant was 80 particles per ml. compared with an average count of 238 particles per ml. given by the seven original

samples. The differential counts remained approximately the same.

Chemical Analyses of Dust.—A chemical analysis of the dust obtained from the rafters in the carding room was undertaken by the Government chemist. The determination of its free silica content was done by treating the ash with alternate cold dilute acid and hot dilute alkali. The soluble portion of the ash was found to be 7·6% of the total dust sample, and petrological examination by Dr. Pulfrey, of the Mines and Geological Department, showed that it consisted mostly of amorphous silica. The insoluble part of the ash, which was 4·2% of the total sample, was found on petrological examination to contain a great deal of felspar and very little quartz. It can be accepted therefore that the quartz content of the dust was very low, and was unlikely to be of consequence as a cause of gross lung damage in the workers.

Investigation of the Workers

An investigation was next undertaken amongst certain of the workers to determine whether sisal dust produced disability or radiological evidence of pulmonary disease. For this purpose 93 persons, in three groups, were chosen from the factory records for investigation. The first group (37) had worked for six months or over in the carding room only. The second group (27) had worked for 10 years or over in other departments of the factory only, and the third group (29) had worked a total period of over two and a half years in the factory and had been employed for some of this time in the carding room. Inadvertently three persons, whose factory service was considerably less than two and a half years, were included in this latter group. Table 3 shows the average length of service and ages of the 93 workers selected.

TABLE 3

AVERAGE LENGTH OF SERVICE IN CARDING ROOM AND IN OTHER DEPARTMENTS OF 93 WORKERS SELECTED FOR EXAMINATION

Time Worked in Carding Room (months)	No. of Workers	Average Length of Service (months)		Average Age (years)
		Carding Room	Other Departments	
0-5	9	2·7	35·4	35·1
6-23	15	13·3	19·6	35·0
24-47	24	30·8	9·4	35·5
48-71	6	59·2	12·7	40·7
72-95	5	83·0	6·3	36·8
Over 95	7	122·4	0	39·1
All who had worked in carding room	66	39·5	15	35·3
Never worked in carding room	27	0	149·4	38·8

It will be observed that although those 27 workers who had never been employed in the carding room had a much longer service in the factory than had the others, the estimated ages in the two groups were much the same. This raises the whole problem of age determination in Africans which is difficult because so few are aware of their exact age. Ages therefore almost always have to be assessed, and this introduces an added source of error not usually present in this type of investigation. In the present study all ages were assessed by the author, and any error is therefore likely to be random, and should not invalidate the comparison between the groups examined. It may well affect a comparison with other groups of workers.

Medical Examination of Selected Workers.—A full history of the length of employment and the type of work performed in the factory of each of the 93 selected subjects was obtained from the factory record sheets, and from these it was also possible to determine the amount of leave taken or other broken duty occurring during each man's service. In addition an industrial history before engagement in the factory was obtained from each man's record of employment kept in the Central Registration Office in Nairobi. In no case was a history of contact with other potentially harmful dusts obtained.

Every person was radiographed, and the maximum breathing capacity (M.B.C.), the vital capacity, and sisal sensitivity tests were carried out on certain of the subjects. A clinical examination was not undertaken unless there was some abnormality in the radiograph as it was believed that the time expended on this would not be commensurate with the benefit gained.

Measurement of Ventilatory Capacity.—An attempt to assess the pulmonary sufficiency of certain of the 93 workers was made by measuring their vital and maximum breathing capacities. The vital capacity was determined with a water spirometer, and the best of three readings was recorded. The M.B.C. was measured on a gas meter spirometer into which the subject breathed to his maximum capacity for one minute timed on a stopwatch. The best of two readings was recorded, and as no fixed rate of breathing was insisted on each subject was allowed to breathe as he liked. It was evident that the effort of breathing for one minute was too much for many of the subjects, and it is certain that in future investigations of this type on Africans a much shorter time limit should be imposed. Owing to the fact that the water spirometer broke, and to certain difficulties in contacting the men, it was only possible to measure the vital capacity in 51 of the subjects, and the M.B.C. on 81 of them. There was,

however, no special selection of cases on which either test was performed. The subjects were all tested before they were radiographed and before they could be identified individually or collectively with their particular jobs. In this way any bias which might have affected the readings was eliminated. The coefficient of correlation between the M.B.C. and vital capacity in 51 subjects on whom they were both performed was +0·492, and although this was not considered very good it was thought worth while enquiring further into the results of each of the two tests.

TABLE 4

MEAN VITAL AND MAXIMUM BREATHING CAPACITIES OF WORKERS WITH TWO YEARS' AND OVER AND UNDER TWO YEARS' EXPERIENCE IN THE CARDING ROOM, AND NO EXPERIENCE IN THE CARDING ROOM

Time Worked in Carding Room	Vital Capacity (l.)			Maximum Breathing Capacity (l./min.)		
	No. Tested	Average Age	Mean	No. Tested	Average Age	Mean
24 months or or over	23	38·3	2·60	36	38·6	52·56
Under 24 months	11	36·5	2·65	20	36·2	55·74
Never worked	17	38·0	3·07	25	38·5	61·1

It was found that the measurement of the vital capacity of those 23 workers who had worked in the carding room for two years or over was significantly lower than the average of those 17 workers who had never worked in the carding room. (The observed mean difference was 2·6 times the standard error of difference.) On the other hand, there was no significant difference between the mean vital capacities of those with over two years' service and those 11 workers with under two years service in the carding room. The latter group, like those with longer service in the carding room, showed a significantly lower vital capacity than the group who had never worked in the carding room. (The observed mean difference was 2·2 times the standard error of difference.)

The numbers are small, and the results therefore open to some doubt; but the same tendency is observed when the results of the maximum breathing capacities are studied. In this instance it was found that the only significant difference was shown between the M.B.C. of those persons who had worked two years or over in the carding room and those who had never worked in the carding room. (The observed difference between the means was 2·5 times the standard error.) There was no significance in the difference between the M.B.C. of those with under two years' service and those with longer service in the carding room; or between those with under two years' service in the carding room and those with no service in it at all.

It will be observed from Table 4 that the average apparent ages of the workers in each group were very similar, and the results in this respect are therefore comparable. The findings suggest that persons who have worked in the carding room for two years or over have a significantly lower pulmonary function than those who have never worked in the carding room.

Sisal Sensitivity Tests.—Although it did not appear, either from the history or the medical records, that workers in the carding room were subject to allergic pulmonary manifestations, it was considered of interest to determine whether there was any special sensitivity shown by them to intradermal injections of sisal extract.

Two extracts of sisal dust, one prepared from the rafters in the factory (M.R.L.), and one prepared from dust taken from a different factory (H.B.), were injected intracutaneously into the forearms of some of the workers selected for radiological examination. The results, which were read 15-30 minutes after an injection of 0·1 ml., are given in Table 5.

TABLE 5

INTRADERMAL SENSITIVITY TESTS PERFORMED WITH TWO SISAL EXTRACTS ON WORKERS WITH OVER SIX MONTHS' EXPERIENCE IN THE CARDING ROOM AND ON WORKERS WITH NO EXPERIENCE IN THE CARDING ROOM OR FOR UNDER SIX MONTHS

	Extract	No. Tested	Mean Induration (mm.)
Workers with over 6 months in carding room	HB	45	10·27
	MRL	24	10·93
Workers with no experience, or under 6 months in carding room	HB	19	8·5
	MRL	17	11·9

It will be observed from the results of these tests that workers exposed to sisal did not show any peculiar reaction to it, and indeed it was found that a similar type and grade of reaction was observed amongst some of the African general hospital population who had never been exposed to sisal. Cayton, Furness, and Maitland (1952) had a similar experience when skin testing cotton dust extracts. The reaction of those with byssinosis did not differ from that of the adult urban population not specifically exposed to cotton dust.

Radiological Investigation.—A postero-anterior radiograph was taken of each of the 93 workers. Each radiograph was viewed by three assessors, sitting separately and unaware of any relevant particulars about the subject. In the interpretation of the radiographs each assessor was asked to pay particular attention to the presence of early or late stages of pneumoconiosis, especially pulmonary

samples. The differential counts remained approximately the same.

Chemical Analyses of Dust.—A chemical analysis of the dust obtained from the rafters in the carding room was undertaken by the Government chemist. The determination of its free silica content was done by treating the ash with alternate cold dilute acid and hot dilute alkali. The soluble portion of the ash was found to be 7·6% of the total dust sample, and petrological examination by Dr. Pulfrey, of the Mines and Geological Department, showed that it consisted mostly of amorphous silica. The insoluble part of the ash, which was 4·2% of the total sample, was found on petrological examination to contain a great deal of felspar and very little quartz. It can be accepted therefore that the quartz content of the dust was very low, and was unlikely to be of consequence as a cause of gross lung damage in the workers.

Investigation of the Workers

An investigation was next undertaken amongst certain of the workers to determine whether sisal dust produced disability or radiological evidence of pulmonary disease. For this purpose 93 persons, in three groups, were chosen from the factory records for investigation. The first group (37) had worked for six months or over in the carding room only. The second group (27) had worked for 10 years or over in other departments of the factory only, and the third group (29) had worked a total period of over two and a half years in the factory and had been employed for some of this time in the carding room. Inadvertently three persons, whose factory service was considerably less than two and a half years, were included in this latter group. Table 3 shows the average length of service and ages of the 93 workers selected.

TABLE 3

AVERAGE LENGTH OF SERVICE IN CARDING ROOM AND IN OTHER DEPARTMENTS OF 93 WORKERS SELECTED FOR EXAMINATION

Time Worked in Carding Room (months)	No. of Workers	Average Length of Service (months)		Average Age (years)
		Carding Room	Other Departments	
0-5	9	2·7	35·4	35·1
6-23	15	13·3	19·6	35·0
24-47	24	30·8	9·4	35·5
48-71	6	59·2	12·7	40·7
72-95	5	83·0	6·3	36·8
Over 95	7	122·4	0	39·1
All who had worked in carding room	66	39·5	15	35·3
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however, no special selection of cases on which either test was performed. The subjects were all tested before they were radiographed and before they could be identified individually or collectively with their particular jobs. In this way any bias which might have affected the readings was eliminated. The coefficient of correlation between the M.B.C. and vital capacity in 51 subjects on whom they were both performed was +0·492, and although this was not considered very good it was thought worth while enquiring further into the results of each of the two tests.

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The numbers are small, and the results therefore open to some doubt; but the same tendency is observed when the results of the maximum breathing capacities are studied. In this instance it was found that the only significant difference was shown between the M.B.C. of those persons who had worked two years or over in the carding room and those who had never worked in the carding room. (The observed difference between the means was 2·5 times the standard error.) There was no significance in the difference between the M.B.C. of those with under two years' service and those with longer service in the carding room; or between those with under two years' service in the carding room and those with no service in it at all.

It will be observed from Table 4 that the average apparent ages of the workers in each group were very similar, and the results in this respect are therefore comparable. The findings suggest that persons who have worked in the carding room for two years or over have a significantly lower pulmonary function than those who have never worked in the carding room.

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Radiological Investigation.—A postero-anterior radiograph was taken of each of the 93 workers. Each radiograph was viewed by three assessors, sitting separately and unaware of any relevant particulars about the subject. In the interpretation of the radiographs each assessor was asked to pay particular attention to the presence of early or late stages of pneumoconiosis, especially pulmonary

reticulation, nodulation, and fibrosis. The reports of all three observers were the same for 61 films. In 26 instances the reports of two of the observers agreed, and for the purpose of this investigation the majority opinion was accepted. Differing reports from each of the three observers were obtained for six films, and a final decision on these films was arrived at by discussion between two observers sitting together. The differences which occurred in the interpretation of the radiographs were of a relatively minor degree only, and the reading of the films was consistent when moderate or gross abnormalities were present.

Table 6 shows the radiological findings in workers classified in the three occupational groups. Sixty-five radiographs were classified as showing no detectable abnormality, four showed apical pulmonary fibrosis, three showed appearances of heavy lung markings and linear striation, 13 showed evidence of pleural or diaphragmatic adhesions, and eight films showed evidence of other abnormalities.

Cases with Apical Pulmonary Fibrosis.—The four cases showing apical pulmonary fibrosis present an interesting problem. They all occurred amongst those who had only worked in the carding room.

A more detailed analysis of the exposure times of these four cases shows that their average exposure to dust in the factory was six and three-quarter years compared with four and a half years for all those who had served in the carding room only, and three and a quarter years for all those who had at any time served in the carding room. Of further interest is the fact that no case of apical fibrosis was observed amongst those 23 persons who had been exposed to dust in the carding room for under two years. On the other hand, all four cases were amongst those 43 persons who had served in the carding room for a period of two years or over, whereas three of them were amongst those 18 operatives with four years' exposure or over, and two amongst those five persons who had been exposed from nine to 15 years. This association between length of exposure and radiological findings of apical fibrosis was found to be just statistically significant ($P = 0.05$).

All four cases of apical fibrosis were admitted to hospital and investigated, and their case histories are given below:

Case 1.—S. H., a male Kikuyu, was aged about 58 years.

This man had previously worked about 10 years in the fields planting sisal, and had not been exposed to sisal dust in the brushing rooms. After leaving this work he had been employed for 11 years in his present job working on a teazer card. During this period he had been absent on leave from his job for only two months.

He stated that he had had intermittent attacks of coughing for many years. These took the form of two

TABLE 6

SUMMARY OF RADIOLOGICAL FINDINGS IN (*a*) OPERATIVES EMPLOYED ALL THEIR TIME IN CARDING ROOM, (*b*) IN BOTH CARDING ROOM AND OTHER DEPARTMENTS, AND (*c*) ONLY IN OTHER DEPARTMENTS

Time (mth.) Worked in Factory	Departments Worked in	No. of Workers	Average Age	Radiological Findings					Average Total Time Worked in Factory (mth.)	Average Total Time Worked in Card Room (mth.)
				Apical Fibrosis	Linear Striation	Adhesions	Other Abnormalities	No Abnormality		
0–23	Card room only	5	33·0	0	0	1	1*	3	10·6	10·6
	Card room and other departments	3	33·0	0	0	0	0	3	11·0	3·7
	Other departments only	0	–	–	–	–	–	–	–	–
24–47	Card room only	18	39·1	1	1	3	2*	11	30·9	30·9
	Card room and other departments	13	33·1	0	0	1	0	12	34·0	15·8
	Other departments only	0	–	–	–	–	–	–	–	–
48–71	Card room only	4	39·5	1	0	1	0	2	62·25	62·25
	Card room and other departments	5	39·2	0	0	2	2†	1	64·6	22·0
	Other departments only	0	–	–	–	–	–	–	–	–
72–95	Card room only	3	35·0	0	0	1	0	2	91·7	91·7
	Card room and other departments	5	37·8	0	0	1	1‡	3	79·6	22·6
	Other departments only	0	–	–	–	–	–	–	–	–
95 and over	Card room only	7	46·7	2	1	0	0	4	111	111
	Card room and other departments	3	36·0	0	0	1	0	2	121·3	55·7
	Other departments	27	38·8	0	1	2	2§	22	149·4	–

* Calcified foci in lung fields. † One case of pulmonary tuberculosis and one case with transient infiltration.
‡ One case of left ventricular hypertrophy. § One case with transient infiltration, and one case of cervical ribs.

or three months of bad coughing followed by two or three months relatively free of it. He was in the habit of spitting up considerable amounts of greenish sputum but had never had any haemoptyses or blood-stained sputum. He had never had asthma or bronchitic symptoms when exposed to sisal, and had only once been in hospital (on account of an accident to his finger).

Clinical examination showed that he had slight clubbing of the fingers, poor chest expansion, and persistent crepitations at the left apex. He was apyrexial. His urine was normal, and the blood slide was negative for parasites. The Mantoux test (10 T.U. old tuberculin) was positive after 72 hours. The E.S.R. (Wintrobe) was 18 mm. per hour, and the haemoglobin (Sahli) was 95%. The total white count was 7,250 cells per c.mm. (polymorphs 50%, lymphocytes 44%, large mononuclears 1%, and eosinophils 5%).

The sputum was copious and semi-purulent, and contained some black streaky flecks. Microscopic examination showed many polymorphs and mononuclears packed with light brownish granules which under the polarizing microscope showed the same birefractive pattern as did the sisal dust. The prussian blue reaction was negative, and no tubercle bacilli or fungi were seen. Culture of the sputum for fungi on Sabouraud's medium on eight occasions failed to produce any growth, and eight cultures for tubercle bacilli on Löwenstein-Jensen medium gave no growth. Guinea-pig inoculation on two separate occasions produced no tuberculous lesions in the pigs.

The vital capacity was 1,800 ml., and the M.B.C. was 57 litres per minute. The H.B. sisal extract gave an induration of 10 mm. a quarter of an hour after injection. An E.C.G. showed no abnormality.

The straight radiograph showed pleural thickening over both upper zones which was more marked on the left. There was evidence of bilateral fibrosis, atelectasis, and possibly cavitation at both apices, the appearances being more marked on the left. The tomogram showed that the pulmonary fibrosis was situated posteriorly at both apices, and was maximal at the 8 cm. cut. A bronchogram of the left apex showed crowded left apical bronchi with a moderate degree of dilatation, and there was marked distortion and deviation of the trachea.

A bronchoscopy was performed and showed no abnormality of the right upper, middle, and lower lobe bronchi. The left upper bronchus was slightly red and congested, and contained mucopus of which swabs were taken and cultured for both tubercle bacilli and fungi with negative results.

This man returned to the factory to work and was given another job in the finishing store where he was exposed to no dust. Follow-up straight radiographs taken 16 and 22 months later showed no change in the radiological picture, and the sputum was still negative for tubercle bacilli after concentration. He now says that he has an occasional cough but feels quite fit.

Case 2.—K. N., a male Mkamba, was aged about 58.

Before his present employment he had worked for many years planting sisal in the fields. He was then engaged as a headman on a coffee estate for three years, after which he started his present job in the carding room where he had been employed on a teazer card for nine years. He had had only one month's leave away from work during the whole of this period.

He complained that he had had a productive cough for a long time and much sputum. He had been in hospital for six days about two years previously with an illness which was diagnosed as a right basal lobar pneumonia. No radiograph had been taken at this time. He had no history of haemoptysis or any allergic susceptibility to sisal dust.

Clinical examination showed he had early clubbing of the fingers, poor respiratory excursion, and bronchial breathing over the left apex and mid zone. No abnormalities were detected in the urine, and the blood slide was negative for parasites. The Mantoux test (10 T.U. old tuberculin) was positive after 72 hours. The E.S.R. (Wintrobe) was 12 mm. per hour, and the haemoglobin (Sahli) was 100%. The total white count was 5,800 cells per c.mm. (polymorphs 38%, lymphocytes 57%, and eosinophils 5%).

The sputum was copious and semipurulent. On microscopic examination many polymorphs and mononuclears were seen packed with small brown opacities which showed the same birefractive pattern under the polarizing microscope. The prussian blue reaction was negative, culture for fungi on Sabouraud's medium on seven occasions gave no growth, and culture for tubercle bacilli on seven occasions on Löwenstein-Jensen medium also failed to grow organisms. Inoculation of the sputum into guinea-pigs on two occasions failed to produce any lesions.

The vital capacity was 1,900 ml., and the M.B.C. 34·5 litres per minute. The H.B. sisal extract showed an induration of 5·5 mm. 15 minutes after injection. The E.C.G. showed notching of the Q.R.S. complex, and S.T. elevation in lead VI but otherwise no abnormalities.

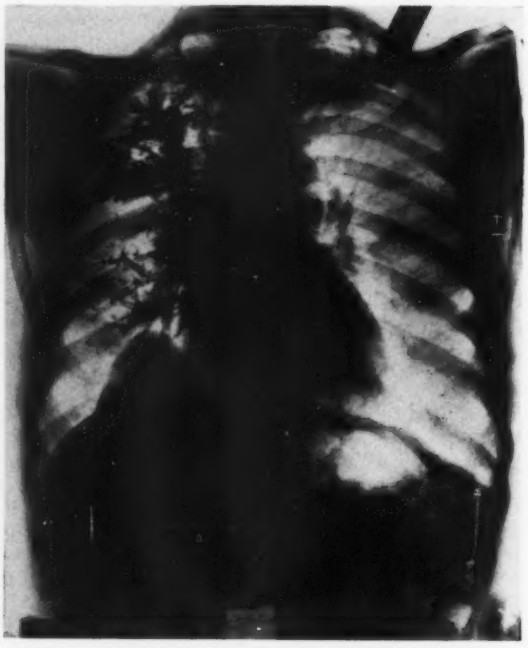
The straight radiograph (Fig. 3) showed pleural thickening over a fibrosed and partially atelectatic right upper lobe. There was considerable bowing of the trachea to the right, and the lesser fissure was displaced upwards. The tomogram showed that the fibrosis was situated posteriorly in the apex of the right lung, and was most marked at the 6 cm. cut. A bronchogram (Fig. 4) showed a moderate diffuse bronchial dilatation with crowding in the right upper lobe.

Bronchoscopy showed that the left bronchial tree was very pale and atrophic, and contained a number of dry crusts. The appearances in the right bronchial tree were very different and were most marked about the right upper lobe bronchus. The mucosa here was thick, red, and congested, and the bronchi contained much mucopus. Swabs from the left and right upper lobe bronchi were cultured for fungi and tubercle bacilli with negative results.

He returned to work in the finishing store where he was no longer exposed to dust. Follow-up radiographs taken 16 and 22 months later showed no radiographic change, and the sputum was negative for tubercle bacilli after concentration. He now says that he has no cough and feels quite fit.

Case 3.—R. S., a male Embu, was aged about 48.

This man had previously worked on a sisal estate as a



FIGS. 3 and 4.—Radiograph and bronchogram in Case 2 showing apical pulmonary fibrosis.

herdsman before taking up his present employment as a worker on the carding machines. He had been in this job four and three-quarter years, and almost all of this time had been spent on the breaker card, but for a short period he had been working on a teazer card. During the whole of this period he had spent a total of three weeks away from work.

He had recently noticed that he had been becoming more breathless than usual, and he also complained of a an unproductive cough. He had never been admitted to hospital, and had no history of asthmatic attacks, allergy, or haemoptysis.

On examination he had clubbing of the fingers, fair respiratory excursion, and bronchial breathing was detected at the right apex at the back. No abnormalities were observed in the urine, and the blood slide was negative for parasites. The Mantoux test (10 T.U. old tuberculin) was positive after 72 hours. The E.S.R. (Wintrobe) was 7 mm. in one hour, and the haemoglobin (Sahli) was 95%. The total white count was 4,100 cells per c.mm. (polymorphs 52%, lymphocytes 33%, mononuclears 1%, and eosinophils 14%).

The sputum was negative for fungi and tubercle bacilli on microscopical examination, and culture on Sabouraud's and Löwenstein-Jensen media on seven occasions each gave no growth of fungi or tubercle bacilli. Two guinea-pigs were inoculated with sputum and neither developed tuberculous lesions.

The M.B.C. was 39 litres per minute, and the skin sensitivity test for sisal (H.B. extract) showed an induration of 10 mm. after 15 minutes. A sigmoidoscopy, performed because of complaints of passing blood in the stools, showed nothing abnormal, and a rectal biopsy showed no ova.

The straight radiograph showed right upper lobe fibrosis with marked deviation of the trachea to the right and considerable displacement of the lesser fissure upwards. There was a right diaphragmatic adhesion. The tomogram indicated that the fibrosis was mostly situated in the posterior part of the right upper lobe, being maximal at the 8 cm. cut. The bronchogram was a failure because of inadequate filling, but small, probably bronchiectatic, cavities were observed in the tomogram.

A bronchoscopy was performed and no abnormal appearances were detected. Swabs from the left and right main bronchi were cultured for tubercle bacilli with negative results.

After returning to the factory he refused to change his job in the carding room for another because it was more remunerative. By this time the dust extraction plant had been installed, and the dust concentrations in the carding room were very low. Follow-up radiographs 10 and 22 months later showed no radiological change, and the sputum was negative for tubercle bacilli after concentration. He now says that he occasionally coughs up a little sputum but feels quite fit.

Case 4.—M. M., a male Jaluo, was aged about 49. This man had previously been engaged as a farm labourer for three years, he had then worked as a cutter on a sisal estate for another three years. He started his present job in the carding room two years previously, and had been employed for three-quarters of the time on batching and for the rest of the time on a breaker card

machine. He had spent two weeks on leave away from his job.

He complained of a cough, and this he thought had started about 10 months previously after an acute illness accompanied by a severe cough. He did not go to hospital during this illness but had twice previously been in hospital with chest complaints. He had no history of asthma, allergic phenomena, or haemoptysis.

On examination there was doubtful finger clubbing, and his chest expansion was only fair, but otherwise no abnormality was found. His urine was normal and his blood slide was negative for parasites. The Mantoux test (10 T.U. old tuberculin) was positive after 72 hours. The sedimentation rate (Wintrobe) was 6 mm. in one hour, and his haemoglobin (Sahli) was 110%. The white blood count was 4,500 cells per c.mm. (polymorphs 42%, lymphocytes 52%, and eosinophils 6%).

The sputum was mucopurulent and scanty, and on microscopical examination was negative for fungi and tubercle bacilli. Culture of the sputum on Sabouraud's and Löwenstein-Jensen media on six occasions each produced no fungi or tubercle bacilli. Guinea-pig inoculation of the sputum on two occasions was negative for tuberculosis.

His M.B.C. was 31 litres per minute, and sisal sensitivity tests with H.B. extract showed an induration of 8·5 mm. 15 minutes after the injection.

The straight radiograph showed a streaky fibrosis of the right upper lobe, and to a lesser degree in the left upper lobe. There were also right diaphragmatic adhesions, and the lesser fissure was displaced upwards. The tomogram showed that the fibrosis was most marked in the posterior parts of both upper lobes, and was maximal in the 6½ cm. cut. A bronchogram of the right upper lobe showed deviation of the trachea to the right, crowding of the bronchi, and bronchiectasis.

He returned to work and was transferred to the new factory where he was no longer exposed to dust. Unfortunately he left this job a year later and could not be traced for follow-up radiographs.

The symptoms and physical signs of these four cases have in common cough, clubbing of the fingers, and signs of emphysema. The M.B.C. and vital capacities were low when compared with those of other workers of the same age and experience. The sputum of every case was consistently negative for tubercle bacilli on direct examination, culture, and guinea-pig inoculation, and in two cases in which it was examined for dust particles it was found to contain numerous intracellular foreign bodies which were similar to sisal dust under the polarizing microscope—an observation of some interest in that it indicates a degree of tissue reaction to the dust. The radiological pictures presented by the cases were also similar in many respects. The fibrosis was situated at the apex, was bilateral in two cases, was maximal in the posterior part of the lung, and tended to be concentrated at the periphery in the pleural and subpleural spaces. Crowding of the bronchi and evidence of bronchiectasis was observed in three patients, and was strongly suspected in the fourth from whom a bronchogram was not obtained. The similarity of the clinical and radiological picture presented by these cases makes one suspect that they have a common aetiological basis.

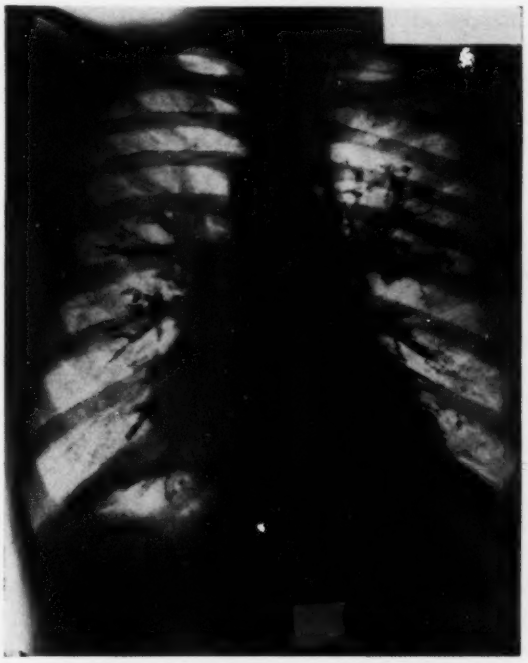


FIG. 5.—Bronchogram showing varicose dilatation of both lower lobe bronchi.

Cases with Heavy Lung Markings and Linear Striation.—Of those three subjects whose radiographs showed evidence of heavy lung markings and linear striation the first had worked for eight years in the carding room. His radiograph showed an increased striation at both bases which was noted by all three assessors. The man had clubbing of the fingers and symptoms suggesting bronchiectasis. A bronchogram (Fig. 5) revealed varicose dilatation of both lower lobe bronchi. Whilst the association of bronchiectasis with sisal dust must be problematical it should be noted that all four cases of apical fibrosis also showed bronchiectasis, and that similar cases have been described as a chronic sequel to bagassosis.

The second case had had 13 months' previous experience in the brushing room of a sisal estate factory elsewhere, and his total exposure to sisal dust was three and a half years. The radiograph showed a streaky linear mottling in both lung fields which was commented on by two assessors. He

complained of no symptoms and showed no physical signs. A full investigation in hospital, including a bronchogram and sputum culture, failed to reveal any other abnormalities. The third and last case in this group was a man who had worked 12 years in the rope-making plant, and had been engaged on a machine which produced a small amount of sisal dust, but nothing comparable to that generated in the carding room. Two assessors reported that his radiograph showed bilateral fine reticulation. He had no symptoms, and clinical and other investigations in hospital, including a bronchogram and sputum culture, showed no further abnormality. The radiographs of the latter two cases could well pass as showing evidence of the earliest stages of dust reticulation but the appearances were so indefinite that it was difficult to make a confident diagnosis.

After investigation in hospital the two patients who had previously been working in the carding room returned to work in other departments in the factory where they were not exposed to dust. The third patient returned to his old work in the rope-making plant. A follow-up of all three cases over a period of 20 months has shown no change in the radiological pictures, and all say now that they are quite fit except for an occasional cough.

Pleural or Diaphragmatic Adhesions.—In no instance did the adhesions seen radiologically appear to be very extensive. In seven cases they were recorded as diaphragmatic, in four cases as costophrenic, and in two as pleuropericardial. There was nothing to indicate anything particularly specific about the radiological appearances, and it is considered that they were merely indicative of some previous respiratory infection.

It will be seen from Table 6 that adhesions were observed in six radiographs out of the 33 taken of persons who had worked in the carding room only (excluding the four cases of apical pulmonary fibrosis). They were observed in five radiographs out of the 29 taken of persons who had worked both in the carding room and other departments, and in two out of the 27 taken of persons who had never worked in the carding room. They were therefore two to three times as commonly observed in the radiographs of persons who had worked in the carding room as in those of persons who had not, and although this is not statistically significant ($P = 0{\cdot}3$), the finding is consistent with the observation that both respiratory infections and lobar pneumonia appeared to be commoner amongst carding room operatives.

Radiographs Showing Other Abnormalities.—Eight workers had radiographs showing various abnormalities which did not appear to be connected with dust exposure. A case of pulmonary tuberculosis was found which was proven bacteriologically and apparently uncomplicated by other pulmonary disease. The radiographs of two persons showed small pulmonary infiltrations which on further follow-up proved to be transient. One further radiograph showed left ventricular hypertrophy, another showed cervical ribs, and three showed calcified foci.

Further Investigations Carried Out in Three Sisal Estate Factories

An endeavour was made to extend the investigations undertaken in the sisal bag factory by carrying out a similar type of survey amongst workers in the brushing rooms of three sisal estate factories. These three estates (*A*, *E*, and *R*) were chosen because of the relatively low labour turnover which they were reported to have, and because of their proximity to facilities for radiography; but even so it was necessary to transport the workers from one estate a distance of 23 miles for radiological examination.

The investigations carried out in the three estates were purposely made as simple as possible. A radiological examination of the chest was performed on all available workers in the brushing rooms, ensuring that those with the longest service were included. The industrial history of each man examined was obtained, and this was checked with the estate records when these were available, and also with records at the Central Registration Office. It was found impossible to assess sick rates amongst the employees as none of the estates kept sick registers. Dust samples were taken with a thermal precipitator in each factory.

Dust Concentrations.—The dust in sisal estate factories is mainly generated by the brushing machines which, acting as carding machines with blunt combs, clean the decorticated fibre which is fed to them by hand. Exhaust ventilation was not installed in any of the factories investigated but as each was open sided on at least one and a half sides some natural ventilation was available.

The employees worked on a piecework system, and their total daily exposure to sisal dust ranged between four and six hours. It was obvious to the naked eye that those exposed to the maximum amount of dust were engaged on operating the carding or brushing machines; on the other hand, those engaged on baling and packing the fibre were exposed to minimal quantities of dust, and those working on sorting and grading the fibre were exposed to intermediate concentrations. These observations were confirmed by the results of the

dust samples (Table 7). The majority of samples were taken from around the brushing machines where those engaged on brushing, sorting, and grading worked, and a few were taken distal to the brushing machines from areas where those engaged on baling and packing worked.

TABLE 7

AVERAGE DUST CONCENTRATIONS IN THREE SISAL ESTATE FACTORIES TAKEN FROM POSITIONS NEAR AND DISTAL TO BRUSHING MACHINES

	Proximal to Brushing Machines		Distal to Brushing Machines	
	No. Samples	Average Count (particles/ml. 0·5-5μ)	No. Samples	Average Count (particles/ml. 0·5-5μ)
Factory *A*	3	284	1	60
Factory *E*	5	96	1	24
Factory *R*	2	126	1	30

The high concentration of dust around the brushing machines in factory *A* was due to the fact that the machines were situated in the centre of the room and thus all the dust generated by them was liberated directly into the room. The machines in factories *E* and *R* were, on the other hand, situated on a side wall and consequently much of the dust from them was blown outside.

Exposure Time of Workers Examined.—Seventy-six workers in all three factories were radiographed; 32 of these persons worked as brushers or carders, 30 as sorting and grading operatives, and 14 in baling and packing operations. Table 8 shows the average exposure time to dust of these workers, and it will be noted that not only was the total time worked less than that amongst the workers in the sisal bag factory but also the exposure time of each individual each day was about half that in the sisal bag factory.

TABLE 8

AVERAGE LENGTH OF SERVICE OF WORKERS EXAMINED IN FACTORIES *A*, *E*, AND *R* ENGAGED IN BRUSHING AND CARDING, SORTING AND GRADING, AND BALING AND PACKING

	No Workers	Average Time Employed (months)	Previous Exposure to Dust (months)*
Brushers and carders	32	33	13·6
Sorters and graders	30	18·4	0·3
Balers and packers	14	39·4	3·4

* Previous exposure to sisal dust was accepted if any worker had worked on carding, brushing, sorting, or grading in any sisal factory.

There was also a considerable difference in the numbers of persons who had been exposed to dust for the longest periods; for whereas there were 16 workers in the sisal bag factory who had worked for four years or more on carding machines there were only five workers in the estate factories who had worked this time on brushing or carding machines. In the only estate factory (*A*) where the dust concentrations were comparable with those in the sisal bag factory, the average daily exposure of the workers to the dust was half, and the total service two-thirds, of that of the workers in the sisal bag factory.

Radiological Abnormalities.—A chest radiograph of each of the 76 employees was taken, and the films were read "blind" by two of the assessors who had previously reported on those from the sisal bag factory. There was agreement in the interpretation of 69 films, and the remaining seven were given to another assessor for an independent reading which was accepted as final. Table 9 classifies the radiological findings, and it will be noted that none of the radiographs showed any evidence of apical pulmonary fibrosis or increased linear striation, but it can be observed that there was the same tendency for adhesions to occur in the films of those who had been most exposed to dust.

TABLE 9

SUMMARY OF RADIOLOGICAL FINDINGS OF 76 PERSONS WORKING IN THREE SISAL ESTATE FACTORIES

	No. of Workers	Adhesions	Other Abnormalities	No Abnormality
Brushers and carders	32	3	4*	25
Sorters and graders	30	1	2†	27
Balers and packers	14	0	2‡	12

* Two cases of pulmonary tuberculosis, 1 calcification, 1 severe scoliosis.
† 1 calcification, 1 old fractured ribs.
‡ 2 calcification.

The information obtained from these investigations was of a generally negative nature, but in view of the relatively low exposure times and low dust concentrations in the sisal estate factories it could hardly be expected that pulmonary disease due to chronic exposure to dust would be found.

Discussion

The four cases of apical fibrosis and bronchiectasis are rather strikingly similar, whereas the other case of basal bronchiectasis, although not radiologically alike, is similar in so far as occupational history and clinical findings are concerned. The occupational histories of these five cases are also similar—an exposure to sisal dust in the carding room of the factory for a number of years. The absence of any detected cases with pulmonary fibrosis or bronchiectasis amongst those who had either only been exposed to dust for short periods, or who had never been exposed to it, but who had, nevertheless, worked for similar or longer periods in other parts of the factory makes it seem probable that long

exposure to heavy concentrations of sisal dust may produce pulmonary damage.

Typically pneumoconiosis is bilateral and relatively symmetrical in the middle and upper zones of the lung fields. In two of the four cases showing apical fibrosis the radiological picture showed these characteristics but in the other two cases the changes were unilateral. But Dunner *et al.* (1946), in their investigation amongst dock labourers exposed to the organic dust of grain and seed, have shown that unilateral radiological changes, including fibrosis, were considerably commoner than bilateral changes.

The radiological appearances of the four workers showing apical fibrosis were not typical of silicosis, but did suggest chronic fibroid tuberculosis. However, it is unusual to find chronic tuberculosis of this type amongst Kenya Africans, and the chances of finding four such cases amongst 93 persons radiographed must be remote. Also guinea-pig inoculations and frequent miscroscopic and cultural examination of the sputa failed to demonstrate any tubercle bacilli.

Apical fibrosis is observed occasionally amongst the general African population of Kenya. But the radiological appearance is not similar to the distribution and type of fibrosis observed in these carding room workers where the fibrotic lesions were patchy but confined to the apices and posterior parts of the lungs, and not necessarily segmental, and tended to involve the pleural and subpleural areas.

Allergic manifestations of both the upper and lower respiratory tract are common in those in contact with organic dusts. Schilling, Hughes, Dingwell-Fordyce, and Gilson (1955) have shown that the asthmatic attacks, suffered by cotton operatives in the card and blow rooms, do not produce fibrosis nor do the radiographs show any characteristic change. No allergic history or the characteristic chest tightness on Mondays of byssinosis was obtained from any of the four cases; or indeed from any worker questioned in the carding room. Nor did an inspection of the sick register reveal any such condition. For what they are worth intradermal skin sensitivity tests with sisal dust showed no special sensitivity by any group of workers. In three cases of pulmonary fibrosis the blood eosinophil count was on the high normal side, 270 to 360 cells per c.mm. (5 to 6%). This was not considered especially remarkable for an average adult African. In the fourth case the count of 570 cells per c.mm. (14%) was high and unexplained.

Hunter and Perry (1946) have described two cases of bilateral fibrosis and bronchiectatic cavitation in men who were working on a bagasse shredder. The sputum of both these cases was consistently negative for tubercle bacilli and fungi, and they were considered to represent a chronic sequel to an earlier attack of bagassosis. These two cases appeared to be in many ways similar to the four cases of apical fibrosis and bronchiectasis and the case of basal bronchiectasis detected in the present survey.

Two of the five cases of bronchiectasis found in the survey gave a past history of an acute pulmonary disease whilst they were exposed to sisal dust, and although it was possible that this may have been an illness similar to the acute phase of bagassosis, the history of the condition given by the patients in retrospect appeared to be typical of pneumonia, and differed from the incapacitating, debilitating, and long-drawn-out disease of acute bagassosis.

It was considered possible that the apparent greater susceptibility of the carding room workers to " pneumonia " was due to an acute infection similar to bagassosis. But a search of the hospital records of carding room workers admitted to hospital with acute respiratory infections did not produce evidence to support this idea.

Hunter (1955) believes that bagassosis is due to a mechanical blocking of the bronchioles with vegetable dust, and it is of some interest to note that the chemical composition of bagasse and sisal dust is similar (Table 10). Other authors, however, believe that bagassosis is a bronchopulmonary mycosis.

TABLE 10

CHEMICAL COMPOSITION OF SISAL AND BAGASSE DUST COMPARED

	Sisal (Government Chemist)	Bagasse (Lemone *et al.*, 1947)
Lignin (%)	38	15
Cellulose (%)	30	55
Pentosans (%)	15	24
Acetic acid (%)	1	6
Moisture (%)	9	—
Ash (%)	12	—

In the majority of cases of bagassosis the acute disease process in the lung resolves completely, and therefore the acute condition is observed more frequently than the chronic. By analogy it would be expected that many of the carding room workers, who were constantly exposed to sisal dust, would suffer acute symptoms. However, no acute respiratory condition similar to bagassosis has been detected in the factory in a retrospective investigation of acute chest conditions, and a continual watch on the employees for the last two years.

The condition found amongst the sisal workers is more similar to the chronic lung condition described by Hunter (1950) amongst workers in the Hungarian pepper industry who were engaged in splitting the pepper by hand. Some of these workers, especially those with many years at the job, developed

apical fibrosis, cavitation, and bronchiectasis. The disease was presumed to be caused by a fungus, *Mucor stolonifer*.

Pulmonary disease caused by fungi can give very much the same radiological and clinical picture as the sisal factory cases. No direct evidence of any such causation was found in these patients as the result of the examination of their sputa, but it should be noted that no bacteriological investigations were carried out on the dust generated in the factory. However, the difficulties of incriminating fungi in pulmonary disease are well known, and it is considered that a fungal origin is the most likely aetiological factor in the four cases of apical fibrosis described. Whatever is the causation of the fibrotic bronchiectatic condition found in these cases it is difficult to avoid the conclusion that a single aetiological agent, which is connected with the inhalation of dust, is responsible.

Summary

A study was made in Kenya in a factory making ropes and bags from sisal to determine whether the dust produced causes pneumoconiosis or other chest diseases.

The average dust concentration in the card rooms was 243 particles per ml. (0·5 to 5μ). Other parts of the factory were relatively dust free. Deposited dust had a very low silica content.

The respiratory illness sickness rate was twice as high in the card-room workers as in those working in other parts of the factory.

Radiographs of 37 workers with between six months' and 15 years' exposure in the card rooms revealed four with a similar type of apical fibrosis. Two showed heavy lung markings. In 46 films of workers of long experience in other parts of the factory only one showed heavy lung markings and none apical fibrosis.

The average maximum breathing capacity (recorded for one minute) was 53 l./min. in 36 card-room workers and 61 l./min. in 25 workers in other parts of the factory and of similar age. The difference is statistically significant.

No worker exposed to sisal dust gave the characteristic history of byssinosis. Skin sensitivity tests with extracts of sisal were uninformative.

A subsidiary radiological survey of men in three sisal estates showed no evidence of pneumoconiosis or apical fibrosis but the exposure of the workers had been short and the dust concentration low.

The apical fibrosis is unlike that seen in the general African population. Intensive investigations for tubercle bacilli were negative.

It seems possible that the fibrosis is related to occupation; its possible relation to the chest disease occurring in workers in bagasse and peppers is discussed

I am most grateful to Dr. P. E. C. Manson-Bahr for providing me with beds in his wards in King George VI Hospital, and to Mr. P. Clifford for performing the bronchoscopies.

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Finally I should like to thank the Labour Commissioner for permission to publish.

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References

Anton, W. (1934). *Med. Klin.*, **30**, 1092.
Caminita, B. H., Baum, W. F., Neal, P. A., and Schneiter, R. (1947). *Publ. Hlth Bull. (Wash.)*, No. 297.
Cayton, H. R., Furness, G., and Maitland, H. B. (1952). *Brit. J. industr. Med.*, **9**, 186.
Dunner, L., Hermon, R., and Bagnall, D. J. T. (1946). *Brit. J. Radiol.*, **19**, 506.
Fawcitt, R. (1936). *Ibid.*, **9**, 172.
Hoffmann, W. (1946). *Schweiz. med. Wschr.*, **76**, 988.
Hunter, D. (1950). *Brit. med. J.*, **1**, 506.
—— (1955). *The Diseases of Occupations*, 1st ed., p. 931. English Universities Press, London.
——, and Perry, K. M. A. (1946). *Brit. J. industr. Med.*, **3**, 64.
Jamison, S. C., and Hopkins, J. (1941). *New Orleans med. surg. J.*, **93**, 580.
Leach, J. (1863). *Lancet*, **2**, 648.
Lemone, D. V., Scott, W. G., Moore, S., and Koven, A. L. (1947). *Radiology*, **49**, 556.
Linko, E. (1947). *Ann. Med. intern. Fenn.*, **36**, 98.
McCormick, W. E., Smith, M., and Marsh, S. P. (1948). *J. industr. Hyg.*, **30**, 43.
Marcandier and Le Chuiton (1928). *Rev. Hyg. Méd. Préventive*, **50**, 672.
Martins, A. F. (1956). *Bull. Inter-African Labour Inst.*, **3**, No. 1, p. 26.
Moll, H. H. (1933). *Lancet*, **1**, 1340.
Najera Angulo, L., and Dantin Gallego, J. (1939). *Arch. Mal. prof.*, **2**, 337.
Ordman, D. (1947). *S. Afr. Med. J.*, **21**, 737.
Schilling, R. S. F. (1956). *Lancet*, **2**, 261.
——, Hughes, J. P. W., Dingwall-Fordyce, I., and Gilson, J. C. (1955). *Brit. J. industr. Med.*, **12**, 217.
Törnell, E. (1946). *Acta med. scand.*, **125**, 191.

Brit. J. industr. Med., 1958, **15**, 38.

HEAT STRESS IN NON-FERROUS FOUNDRIES

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In a previous paper (Turner, 1957) the results of a survey of the thermal environments in non-ferrous foundries were reported, reference was made to the index of heat stress proposed by Belding and Hatch (1955), and an indication was given of how this index could be used to evaluate the severity of the heat stress which might be encountered in foundries. A few observations were reported which showed that the required rate of heat loss by evaporation which was predicted by the index was in fair agreement with the rate observed in a sample of foundry workers.

It has been the purpose of the present study to investigate more closely the correlation between the predicted and observed rates of heat loss by evaporation under typical industrial conditions and to examine the applicability of the heat stress index for the assessment of such conditions.

Methods of Measurement

The observations were made during the summer months in two foundries in which there was a wide variety of working conditions ranging from positions round a large reverberatory furnace in a well ventilated part of the foundry where the exposure to heat was only slight, to other positions in a congested and ill-ventilated region where numerous bale-out furnaces were used and the exposure to heat was severe. Observations were made while the men worked normally for periods of between two and three hours.

Under field conditions it was not possible easily to obtain the weights of the subjects nude before and after each observation. A few such observations were made, however, and there was generally no significant change in the weight of the clothing during the period of work. This is thought to have been due to the fact that the men had been at work for some time before the observations were started, and hence their clothing had already become damp and remained in about the same condition. Thus it was felt that the changes observed in the weights of the clothed subjects could be regarded as indicating the amount of sweat lost by evaporation. Only under the most severe conditions did there appear to be much loss of sweat by dripping.

Each subject was weighed clothed before starting work and again immediately after finishing work. A careful note was taken of all fluid consumed and excreted during the working period and from this information, together with the change in weight during the period, it was possible to calculate the total quantity of fluid lost per hour. Assuming this quantity to represent the amount of sweat evaporated, the rate of heat loss by evaporation was calculated by assuming that the evaporation of 1 litre of sweat absorbs 2,400 British thermal units (B.th.U.), the figure used by Belding and Hatch.

In deriving the equations for the computation of the heat stress index Belding and Hatch calculated the heat exchanges between man and his environment with reference to a " standard man " having a surface area of 20 sq. ft. Hence, in order that observed rates of heat loss by evaporation in the present survey should be strictly comparable with the rates calculated from the equations of Belding and Hatch, the surface area of each subject was calculated by the method of Du Bois and the observed rates of evaporation of sweat were then corrected to apply to an area of 20 sq. ft.

The value of the heat stress index was calculated for each individual exposure. A position was chosen on the floor of the foundry where the exposure to heat was similar to the average exposure of the subject and regular measurements were made in this position, at a height of 4 ft. 6 in., of the wet- and dry-bulb air temperatures, the globe thermometer temperature and the air speed as measured by the kata-thermometer. The value of the heat stress index (H.S.I.) was then calculated from the equations given by Belding and Hatch:—

$$\text{H.S.I.} = \frac{E_{req}}{E_{max}} \times 100, \quad \text{or} \quad \text{H.S.I.} = \frac{E_{req}}{2{,}400} \times 100$$

The second equation was used whenever the value of E_{max} was greater than 2,400.

The quantity E_{req} is the amount of heat which the " standard " man must lose each hour by the evaporation of sweat to maintain his body in thermal balance in the given environment. It may be calculated from a knowledge of the globe thermometer temperature (t_g, °F.), the air speed (V, ft. per min.), and the metabolic rate (M, B.th.u./hr./20 sq.ft.) according to the equation:—

$$E_{req} = (22 + 2\sqrt{V})(t_g - 95) + M.$$

The quantity E_{max} is the amount of heat which would be absorbed if the ambient air in the given environment became saturated with water vapour at a temperature

of 95° F., which was assumed by Belding and Hatch to be the temperature of the skin. It may be calculated as

$$E_{max} = 10{\cdot}3V^{\cdot 4}(42 - VP_a)$$

where VP_a is the ambient vapour pressure, mm. Hg.

E_{max} is equal to 2,400 if 1 litre of sweat is evaporated each hour. Belding and Hatch proposed that this figure should be used in the calculation of the value of the index whenever E_{max} exceeded 2,400, because they held that a rate of sweating of 1 litre an hour was the most that a man should maintain over long periods.

The rate of working of an individual diecaster was variable, and there were also variations in the pattern of activity from one caster to another, due mainly to differences in the size and intricacy of the dies in use. It was impracticable to make direct measurements of the metabolic rate during the whole of each observation, and the inherent variability in the rate of working would have rendered a few accurate measurements over a short period of little value. It has been shown (Turner, 1955) that a practised observer can make subjective appraisals of the severity of manual work with reasonable accuracy and it was decided that, for the purposes of this survey, a single value so obtained for the average metabolic rate of all the casters would suffice. The typical average rate of working appeared to be about 165 Kcal/sq.m./hr., or about 1,200 B.th.u./hr./20 sq.ft., and this latter value has been taken as standard throughout the calculations of E_{req} in these results.

Results

Ten subjects took part in this survey and altogether 98 individual observations were made. The results have been summarized in tabular form below. Table 1 shows the overall mean values and the ranges of the different variables measured, and Table 2 shows the mean values of the observed rate of heat loss by evaporation, the heat stress index, and the outside temperature for various ranges of E_{req}, the rate of heat loss by evaporation required to maintain thermal equilibrium. Also in Table 2 are two indications of the difference between the observed rate of evaporative heat loss and E_{req}.

TABLE 1

THE MEAN VALUES AND RANGES OF THE VARIABLES MEASURED

	Mean	Range
Outside air temperature (°F.) ..	68	52–84
Dry-bulb air temperature at working position (°F.)	79	66–100
Wet-bulb air temperature at working position (°F.)	64	52–77
Globe thermometer temperature at working position (°F.)	100	82–120
Air speed at working position (ft. per min.)	130	50–260
Observed heat loss by evaporation (B.th.u./hr./20 sq. ft.)	1,560	700–2,750
E_{req} (B.th.u./hr./20 sq. ft.)	1,440	630–2,410
Heat stress index	71	26–121

For the comparison of the observed rate of evaporative loss with the value of E_{req}, in Table 2, the latter figure has been taken as standard. Since it is calculated from the measurements of the various thermal factors it is thought that it gives a more exact assessment of the severity of the environment than would be given by the observed rate of evaporative loss, which is based on the more variable and less accurately measured loss of weight.

For each exposure the ratio $\frac{\text{observed heat loss}}{E_{req}}$ was calculated, and the average values of this ratio for the various ranges of E_{req} are given in Table 2. The deviation of the average value from unity indicates the extent of any tendency for the calculated E_{req} to over-estimate or under-estimate the rate of sweating. The scatter of the individual values about the mean for each range is indicated by the root-mean-square deviation of the observed rate from E_{req}, expressed as a percentage of E_{req}, and this is also given in Table 2.

The coefficient of correlation between E_{req} and the observed rate of evaporative heat loss was 0·62.

Discussion

Comparison of the overall mean values of E_{req},

TABLE 2

MEAN VALUES OF VARIABLES WITH REFERENCE TO GIVEN RANGES OF RATE OF EVAPORATIVE HEAT LOSS REQUIRED TO MAINTAIN THERMAL EQUILIBRIUM (E_{req})

Range of E_{req}	No. of Observations	Mean Value of E_{req} (B.th.u./hr./20 sq.ft.) (*a*)	Mean Value of Observed Evaporative Heat Loss (B.th.u./hr./20 sq.ft.) (*b*)	Mean Value of $\left(\frac{\text{Obsd. Loss}}{E_{req}}\right)$	Root-mean-square Deviation of (*a*) from (*b*) (%)	Mean External Temperature (°F.)	Mean Heat Stress Index
600– 799	10	650	1080	1·67	80	61·5	27
800– 999	6	880	950	1·14	18	61·0	37
1000–1199	13	1140	1330	1·16	25	64·5	52
1200–1399	13	1310	1580	1·20	29	67·5	70
1400–1599	23	1500	1670	1·12	27	70·0	88
1600–1799	13	1680	1690	1·0	27	69·0	80
1800–1999	11	1840	1840	1·0	14	77·5	105
2000–2199	7	2070	1940	0·94	14	77·5	101
2200–2399	0	—	—	—	—	—	—
2400–2599	2	2410	2060	0·85	33	82·5	105

and of the observed rates of heat loss by evaporation reveals a fair measure of agreement. The mean value of the observed rate was only 8½% in excess of the mean predicted rate and the mean value of the root-mean-square deviation was 33% (Table 1). If the observations in the two extreme ranges of E_{req} in Table 2 are excluded from the calculations the root-mean-square deviation is reduced to 24%. This represents as good a degree of agreement as can be expected in such experiments.

The subjects were performing their normal task in the foundry. During the course of their work they moved about between the furnace and the die, yet it was only possible to measure the exposure to heat with reference to a single position, which had to be selected to represent the average exposure. Similarly an average value for the metabolic rate had to be taken, although the rate of working was variable and dependent on factors which could not be controlled. An unforeseen change in the temperature of the metal in the furnace, or a breakdown of the coating of the die, could result in a temporary change in activity.

The observed heat loss by evaporation has been calculated from the changes in weight during the working period. It was pointed out earlier that it was only possible to obtain the weights of the subjects clothed, and that this was thought to give a fair measure of the rate of evaporation of sweat.

When one bears in mind these sources of variation in the results, the agreement between the observed and required evaporative heat losses appears to be quite acceptable. There is always a considerable individual variation in the results of any study of heat losses from the human body, even when the observations are made in the laboratory with close control over the climatic conditions, the rate of working, and the precision of the weighing of the subjects. All these factors are much less controllable when surveys are made under normal industrial conditions.

The greatest deviation in the results was apparent at the lowest levels of heat stress where the observations were made in the well ventilated, uncongested part of a foundry on cool and breezy days. These conditions resulted in constantly and widely varying climatic conditions in the foundry. It may also be that the men worked harder in these cooler conditions, but it was impossible to verify this. A slight increase in the rate of working, of, say, 5 Kcal/sq.m./hr. would have increased E_{req} by between 5 and 10% in the lower ranges, and this would have reduced the disparity between the figures for E_{req} and the observed evaporative heat losses.

It will be noted from Table 2 that the disparity between the observed values and the values of E_{req} is least when E_{req} is of the order of 2,000. There is general agreement that the upper acceptable rate of sweating for long periods of work should be 1 litre per hour, or in terms of E_{req}, 2,400. As the environmental conditions approach this level it becomes more difficult to form a reliable subjective impression of the severity of the conditions, and a simple but reliable objective method of assessment is of great value. It is thus gratifying to observe such good agreement between the heat stress index and the observed rate of sweating in this particular region.

There was one occasion during this survey when it was reported that on the previous day conditions had become so hot in the foundry that the diecasters had been unable to work in the afternoon. The weather was slightly cooler on the following day, when observations were made, and the values of the heat stress index measured on that afternoon were all about 100. Again, two days later the men were complaining constantly of the heat in the foundry and on this occasion values in excess of 100 were obtained. Thus it would appear that not only does the index supply a reliable assessment of the severity of the environment in the region of the upper acceptable level, but also that conditions which result in a calculated value for the index of about 100 do, in fact, coincide closely with the upper limit of conditions for normal sustained work.

Summary

The results of 98 individual exposures to the environmental conditions occurring in typical non-ferrous foundries have been reported. A comparison between the rate of heat loss by the evaporation of sweat, as calculated from the Belding-Hatch heat stress index, with the rate observed in the 10 subjects of this investigation has been made. A close agreement between the calculated and observed rates was noted, particularly in the range of environments in which the heat stress reached significant proportions. There was also some evidence to support the view that men will not willingly work for prolonged periods under conditions for which the value of the heat stress index exceeds 100.

The author wishes to express his thanks to Dr. T. Bedford, Director, M.R.C. Environmental Hygiene Research Unit, for his encouragement during this study; and also to the managements and workers in the foundries concerned for their willing participation.

REFERENCES

Belding, H. S., and Hatch, T. F. (1955). Index for Evaluating Heat Stress in terms of Resulting Physiological Strains. *Heat. Pip. Air Condit.*, 27, Aug., p. 129.
Turner, D. (1955). *Brit. J. industr. Med.*, **12**, 237.
—— (1957). *Ibid.*, **14**, 177.

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SOME CLINICAL AND ADMINISTRATIVE ASPECTS OF OCCUPATIONAL HEALTH

BY

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The type of work done by doctors in industry varies enormously. One man may devote most of the working week to what are essentially toxicological problems; another may be mainly concerned with what are collectively known as "hygiene" problems; almost all have varying amounts of clinical work which might be called general practice without therapeutics, or, in some instances, minor casualty procedures. In all these roles there is no lack of help and counsel in published literature and in medical meetings of diverse types. Every doctor has been well grounded in the basic sciences on which these tasks are built. In a British Medical Association publication the doctor in industry will see 13 duties listed as being appropriate to his vocation. Of these, six are almost entirely clinical, three are concerned with hygiene, two mainly demand some knowledge of toxicology, and the remaining two can be loosely called administrative. Only one fourth of one of these duties fails to fall within this rough classification and that is " advice to managements regarding accident prevention " (British Medical Association, 1949).

In reality, if a doctor is going to have anything like a full impact and influence in an industry he must concern himself with much more than these aspects alone. He finds himself entering a field for which there is no set training and in which the common pool of experience is far less fully catalogued. He wonders how far into what is apparently a management field he can go without abandoning his professional status; but he knows, or ought to know, that he cannot keep away completely from controversial ground without becoming totally irrelevant to major issues inside his own organization; the mishandling of these issues may render all his work futile.

The decision has to be made by each man for himself and these thoughts on the subject have been prompted by personal experience in constructing a new medical service, partly whole-time and partly part-time, inside a widely scattered nationalized organization. For a new service the limits have to be defined at the same time as the structure is established. It is stretching the word " welfare ", used in the B.M.A.'s notes, to allow it to appear to provide the answer, but some realistic clarification of the relevance of the doctor to some of these important aspects of modern industry is urgently needed. If this is not done, occupational medicine may expand but the expansion will be uneven and its value unrealized.

It would be possible to talk of many different subjects under the heading of our title. Some present little difficulty and are not considered at all here; environmental medicine and safety work come in this category. The relationship of a medical service to the joint consultative or productivity committees of an industry is omitted because of the wide variations between one industry and another in the nature and scope of these bodies, and the same argument militates against the discussion of accident prevention. Three major subjects have been picked out and on these, it is contended, those in charge of medical services should clarify their positions: (1) Redundancy, (2) non-medical aspects of rehabilitation, and (3) the relationship with legal departments, or legal arrangements made by the employing firm.

The broad thesis is that medical departments, to exert their full influence, must be not only advisory to management but must be an integral advisory part of management, and that such an assumption does not conflict with the professional status or ethical principles of a doctor.

Redundancy

This is a topical problem in most British industries. The word " automation " resounds on every side and is frequently used with that sonority that masks ignorance. It is more often debated than defined and it cannot be defined here because it has come to

cover a whole series of problems, the end-result of which is that the employing firm has more employees than it has jobs. The problems of redundancy stem from many roots: difficulties and changes in market conditions, improvements in organization and methods, development of new machinery; all these and other factors combine to create what looks like being the major issue on the industrial scene.

As part of the problem there is also the question of mobility of the employee. It is helpful to consider this subject under two headings, namely, the general, or policy, aspect, and the particular, or individual case, approach.

General Policy.—Immediately it is suspected that a reorganization is likely, it becomes evident to the employee that redundancy is possible. The first reaction of many is fear. In an industry which has for years followed a conservative development path the security of employment has come to be accepted as part of the natural order of things. Whether this is wise or unwise has nothing to do with the case, it is simply a fact. The consequences of this attitude, and of its sequel, fear of loss of status, will be dealt with under the more particular approach, but here it is necessary only to point out, as is now fairly generally accepted, that the only possible minimizer of those natural anxieties is early and full consultation between management and employees. The good doctor in industry will know from his contacts at all levels how successful or otherwise that consultation is, and it is his clear duty to give the management his views on the point. His function in the maintenance of group morale is never more clearly seen.

One of the important facts of this consultation is that it must be, as far as possible, specific. In other words, certain clear promises have to be made. Apart from specified categories of employees, the principle may well be " first in, last out ", but that is not always easily applied in practice, especially as increased efficiency is usually part of the object. In any case, what are the exceptions to be? Should disabled persons be exempted ? If only some of this group are exempted, how are they to be chosen ? Should a distinction be drawn between married men with families and single men ? There is no method of effective selection that will not lead to some heartburning but at least the lines should be clear so that the ill-effects of suspense are minimized. It is my view that the doctor's advice at this level can be clear. There should be no medically protected categories. Just as disability should not be a bar to suitable employment, so it should not be a shield when hardships fall to be widely borne. It is implicit in this approach that the percentage of registered disabled employed would not be allowed to fall below the required minimum but most industries appear to carry far more than that figure and in any case the larger number of disabled are not registered, though their problems at times of redundancy are no less. Almost all such situations and solutions must, however, contain a " hardship " clause if the industrial relations are not to be completely depersonalized. It is from the operation of this clause, not only against dismissal but against mobility, that much of the doctor's hardest work will come and it is here that his strict and hard-won reputation for impartiality will stand him in good stead. Perhaps this refusal to use any sort of medical umbrella sounds harsh, but it is my view that it must be accepted and that to state the reverse is sentimentality. The need for complete fairness of treatment is so great and its genuineness and visibility is so essential to group morale that the doctor must appreciate its place when he looks at the wider canvas.

There is another aspect of importance which must be borne in mind when considering a re-organization. It is probable that, with a redundancy to be faced, a firm will be loth to seek outside applicants for vacant posts. In other words, the smaller number of jobs which will demand a higher calibre of employee will be filled from inside the organization; quite often it is found that changes have come too suddenly to allow of a gradual maturing towards these more demanding centralized posts. Sometimes this works out better in practice than might be expected but the hazard of the procedure should be clearly seen by a doctor and he should be on hand to advise any who find the pace of the race getting too hot without any delay. Kennedy (1957) has summarized the causes and the early symptoms most clearly and a syndrome, too long unrecognized, should now be regarded as defined.

Individual Cases.—If a hardship clause is to be operated it must be dispassionately used. Nowhere is it more difficult to tell black from white than in the matter of early retirement pensions which the rules of some schemes make available only on ill-health grounds, or sometimes on better terms if the retirement is brought about by illness or injury. What are the limits of valid medical grounds ? Indeed, how far can certain facts be called medically relevant at all ? Cases will illustrate the dilemma as it occurs in this industry. The distinction between illness, particularly psychological illness, and general inefficiency can be extraordinarily difficult but it is dangerous for medical certification to be an easy way out of management problems.

Case 1.—A reorganization was taking place in an area where early retirement pensions were poor except when the retirement was on grounds of ill-health. A senior clerk presented a placement problem in the new plan and yet he had good qualifications for retention by virtue of past service. It was felt that he might not be very efficient in the new scheme of things. The medical facts were that in the past he had had diverse vague complaints such as mucous colitis and coccalgia but at the time of examination he appeared perfectly well, apart from the fact that he was, as he had always been, of an introspective nature. He would have been quite pleased to go out on grounds of ill-health but not under voluntary early retirement, and the management were eager that he should be certified in this way. In spite of this agreement certification was refused and in the event he has been accommodated in the new organization.

Was the refusal correct ? In my opinion it was. There were some medical aspects but these were not sufficiently potent to prevent the individual doing the tasks available for him. In a sense it could be said that the doctor acted against his patient's interests, but if a doctor does only what his patient wants him to do, inside or outside industry, his influence and status will soon go. Similarly, if working inside industry he does only what the management thinks to be expedient, his reputation for impartiality is finished. Nonetheless, it can be extremely difficult finding firm ground to stand on in many cases, and not infrequently a professional colleague, who sees only one side of the picture, will be offended at the stand taken, even when he is most carefully consulted about the matter.

On another occasion it was deemed necessary for a fair number of employees to move to another part of the area as part of a reorganization. There were a few jobs remaining in the old location and it was agreed that those with the longest service could have these posts if they wanted them, the only exception to the priority being those with compelling medical or " welfare " reasons.

Case 2.—A man under supervision for tuberculosis, which was now quiescent, brought a medical certificate in support of his claim. Here again there was no disputing the disability but support for the claim was refused on the grounds that his condition was not a bar to movement and the medical reasons which went with it were no more urgent than the non-medical grounds relied on by men who were not disabled.

Case 3.—Another fairly senior official was informed that he must, as a result of re-organization, move his house about 30 miles. The only theoretical grounds of appeal were medical and he advanced a plea on the ground of his wife's health. She had secondaries in the spine arising from a breast cancer and was undergoing deep *x*-ray and other treatment under a consultant in whom she had great trust. It was argued by the management that any treatment would be available in the proposed new location, but a certificate was thought justified in this case.

The great majority of cases are fairly straightforward and, with goodwill on all sides, can be solved amicably in a way that is patently fair all round. The real difficulty arises when there are mixed organizational, welfare, and medical factors, and no one factor is itself large enough to warrant deviation being based on it. An isolated doctor in his ivory tower cannot hope to elicit or comprehend all the aspects involved and is bound to be either so equivocal in his opinions as to be totally unhelpful, or to be biased in one direction or another.

The insecurity engendered by redundancy is not merely a fear of loss of occupation or even loss of earnings, but is very often a fear of loss of status. The man who has been for years chief clerk of some tiny, independent unit, may not have had much salary, but he has been a person of standing and consequence in his own organization, his own town or village, or in his social activities. He can be compulsorily moved to a larger group without loss of cash, indeed even with promotion, yet may exhibit emotional symptoms, quite often with physical sequelae, which a trained industrial medical officer can do much, by explanation and understanding, to prevent or relieve. It is a commonplace to hear from such individuals, " I wanted to talk to you about it because I knew you were aware of all that went on at work". His belief may be exaggerated but at least it shows that the doctor's attempt to become part of the industry has succeeded. It is my contention that there is far more real work to be done on this aspect of occupational health than there is on the hygienic and toxicological side, and that the development of this work is the most constructive step that can be taken against the psychosomatic diseases which appear to increase even faster than the environmental diseases diminish. It is a recurring, pleasurable surprise, even to those not psychiatrically trained, to discover how much can be achieved by frank discussion of apparently insoluble problems.

Much of what has been said refers to clerical staff but the need for the work is no less on the manual side. A considerable number of people remain faithful to one industry and become jealous of their status within it. The tendency is for larger and more streamlined organizations and the danger of depersonalization is great. There is an important and developing part for a doctor to play, provided he integrates himself with all levels of his organization and provided he learns a new approach to the wide range of quasi-medical problems. He takes a risk in emerging from his chromium to do this but he can

achieve little if he declines, or is refused the hazard. Some of the problems he takes on may rightly be called non-executive functions of an enlightened management but if he will not accept them, no one else may and the historic bitterness between employer and employed is not yet diminished enough to make unhelpful the availability of a fair, neutral, " third force ". The particular problems of each employee are unique in his own estimation, and unless he feels that they have had special, impartial, examination, he will never believe that he has been justly treated. The problems of re-adaptation are individual in exactly the same way. Hardship there will certainly be, but it can be understood and limited. There are many ways of helping and the doctor in industry must be familiar with them. Even when little practical assistance is possible, his moral support should be available freely to all.

Administrative Problems in Rehabilitation

When a man has injured the tendons of his thumb and treatment has progressed to the point where increasing exercise is advantageous, there may be relatively little difficulty in employing him in a fully productive way which is not only helpful to him but also useful to his employers. The same is true of most orthopaedic cases. Unfortunately, limb disabilities form a relatively small part of the rehabilitation problem and in all types of case the actual selection of suitable work is only one of many problems. Every occupational medical service must include some " getting back to work " arrangements. In some cases it has been found possible to provide special workshops, special machinery and other physical facilities, but the first step is to provide the right attitude to rehabilitation inside the industry. Unless that is achieved the material provisions are worthless. It is also important to remember that the right attitude has to be created among the workmen as well as among the employers; a surprising number of resettlement difficulties are caused by colleagues who might be expected to be particularly helpful but whose helpfulness stops short of any infringement of their own alleged rights. In discussing plans with management or men's representatives, great care has to be taken to steer a middle course between the emotional approach and considering employees as financial assets. It is easy to build up a most moving case, especially about the more visible deformities or those in the news for which the general public like to express that emotion which pretends to be sympathy; it is easy to impress with talk of being injured in the company's service, as if the consequences of that were more soul-searing than being injured in any other way. On the other side of the picture, it is impossible to prove financial gains from a rehabilitation programme and even if this could be done it would not be the point at issue. The rehabilitation facilities of an industry, however complex or simple they are, should be open equally to all who can make use of them, irrespective of how they came by their disabilities. In no other way is it possible to avoid the charge that " kissing goes by favour ".

However elaborate or simple a rehabilitation plan is, there are certain problems associated with it which must be faced if the plan is to have any hope of success. As a doctor one hopes for its success but a starry-eyed detachment from such facts of industrial life as " rates for the job ", " promotion by service only ", and the maze of little rules, written and unwritten, existing in every organization will not help. In this industry we were particularly handicapped by a sick pay scheme which, after certain conditions were fulfilled, gave 100% sick pay for 13 weeks to all manual workers, and for longer spells to other grades.

Case 4.—A semi-skilled worker had been absent for about 18 months because of tuberculosis. According to the rules of the sick pay scheme he became entitled, as from a certain date, to a further three months' full sick pay. Shortly before this date he came back with a recommendation that if suitable work could be found he could start on a four-hour day. He was hardly delighted to discover that his pay for working within his physical limitations was about half his pay for remaining on the sick list. Similar cases occurred among clerks on other conditions of service.

Case 5.—A shiftworker was absent on sick pay and when he was seen it was decided that, while he was unfit for his own job, he could do another day-work job which was available. His doctor was quite happy to go on issuing certificates as he was unfit for his normal work. While sick he drew nearly one-third more money than he did when alternatively employed.

It is true that men who can do some useful work should not be drawing sick pay. It is true that rehabilitation is in the patient's physical interests. Nonetheless, contradictions such as these instanced have to be dealt with before there is any hope of success. In our particular case, the relationships with other departments have been happy and it proved possible to pay an employee his sick pay entitlement as his rate while he was at work in these circumstances. Otherwise, the rate for the job applies. In another industry a different compromise has been reached whereby the man is paid the difference between his old and new rate but there is a proviso that he shall not drop more than 10s. a week in a re-adjustment job provided that it is

certified that he should eventually be fit to return to his normal work.

It is not a doctor's job to make decisions about these matters but, especially in a new service, it is his work that will raise the problems and he cannot shrug them aside as being irrelevant to him since their solution is vital to the success of his efforts.

Stewart (1954) makes the statement that every firm employing more than 7,500 on one site should consider the setting up of a special rehabilitation workshop, and it is probably fair to say that every firm of that size should be able to absorb all its own disabled from all causes, with one or two minor special category exceptions. On the other hand, a relatively small proportion of the working population is to be found in such large undertakings and, in spite of many committees and large expenditure by public and voluntary authorities, the replacement of the sick and injured in suitable work is probably the weakest link in the therapeutic chain in this country. There seems no reason to believe that the expenditure of more money or the building of more centres would notably help with this problem. Giving a man a broom and hiding him in a corner is not rehabilitation. Sending a man on a long training course and then not using that training is no better. Far the best place in the recovery stage is the patient's normal workplace and a survey of the system of work is often as important as a job analysis of the patient's particular employment.

Case 6.—A man who worked in a meter repair shop had been off sick for about 18 months with rheumatoid arthritis. He worked with two colleagues—loading, unloading, examining, recording, and stacking meters. The meters weighed only 12-20 lb. on the average, but he was in a wheel-chair and that work was clearly beyond him. It proved possible to persuade his colleagues to re-organize the system of work in such a way that the patient did the sedentary clerking and examining. He came back on this basis and when last seen was fetching and carrying in the same way as before his illness.

He would not have made a satisfactory clerk in any other place and, in any case, the deciding factor in his re-adaptation was almost certainly that it was carried out in his own familiar environment.

If a doctor takes the trouble to learn his own industry and more particularly to become known to the employees and to share his plans and problems with them, there are few insoluble rehabilitation cases and any minor roughness of facilities is more than compensated for by psychological gains.

The management may have to be persuaded that their factory is not being converted into a convalescent home—sickness records of disabled persons are often valuable for this—and the employees have to be persuaded that their hard-won agreements are not being carelessly or dangerously circumvented. The patients, particularly the neurotic group who form a large proportion of placement problems, have to be convinced that ordinary work can be rehabilitation and that once found such work they are expected to do it properly. Minor concessions, such as travel out of rush hours, should be closely watched and whenever possible should be temporary. The strictest precautions against abuse are essential if the value of the facilities is to be appreciated and a long queue outside a works physiotherapy department is the antithesis of a successful rehabilitation programme.

Much stress has been placed on the assessment of physical function in diverse disabilities; a fair amount of work has been done on job analysis; very little attention has been given to the significance of group attitudes to the disabled man. It is on non-medical questions that most rehabilitation programmes run into their worst difficulties.

Relationship with Employing Firm's Legal Arrangements

While it has been emphasized that an industrial medical officer must be an advisory part of management and not just an adviser to management, it must be admitted that the appellation " the management's doctor " is, in many ways, a damaging one. It is widely held, even by professional colleagues outside the industrial field, that in some subtle way the doctor in industry has sold his soul to his employer and is incapable of giving a balanced, independent opinion. This, if it were true, would be a grave state of affairs since it would strike at the very heart of the doctor-patient relationship, which needs to be as unfettered by suspicion in this sphere of work as in any other. The feeling of bitterness, which is often the concomitant of the processes of the law, makes any advice on matters under litigation a dangerous exercise for the doctor. On the other hand, it is not always possible to stand aside from these matters.

Case 7.—A workman sustained an injury which led to a mid-thigh amputation. The circumstances of the accident (not covered by the Factories Acts) were not clear but it appeared that an unsafe system of working had been employed and that the employer's agent was to blame. There had been no contributory negligence by the victim. When the man returned to a suitable job which had been found for him he had a considerable loss of earnings retrospectively and of earning power prospectively. He was a simple soul who was not a paid-up member of his Union and had, surprisingly enough, taken no steps towards a claim in common law. The

financial hardship to the man and his family was considerable.

The course adopted in this case was probably cowardly. Senior professional colleagues were consulted and the variation in their advice was, in any case, more confusing than clarifying, but fortunately, while all this was going on, someone else advised the patient to consult a solicitor.

It is an awkward position for a doctor to be the instigator of litigation but yet the man's need and rights should probably have been an overriding factor.

The position frequently arises that an industrial medical officer is asked to assess a case in which a claim has already been made. He should be confident of his ability to give a fair appraisal but he will learn from experience that, even if a report agreed with the patient's private practitioner is produced, this is one instance where he will never be believed to be truly impartial.

It is my opinion that when the patient in these issues comes from inside the industry, the doctor should come from outside. It is unfortunate that, in some industries, doctors have been engaged to " protect the interests of the management ", and such a position must be avoided at all costs. The attitude of management and men towards these claims appears to be perpetually emotionally charged and it is better to retreat from an impossible situation than to endanger the reputation for independence of mind which is essential to the discharge of occupational health duties.

Conclusion

Much has been written and spoken about the need for an extension of occupational health services. There is available a wealth of published information on most of the diseases associated with industrial processes and much of this information seems to repeat itself in rather tedious cycles. There is, however, very little to guide the newcomer to the industrial field on many matters which he finds to be of much more frequent impact; all too often he is allowed to become irrelevant to the main events in his own industry because of personal diffidence or because of his deliberate abstention from what he considers to be " non-medical " topics. Environmental health facilities will improve; that appears to be a well-established trend. It is, however, not by influence on the physical environment alone that an industrial medical officer should be judged but by his influence on individuals and groups. In the last analysis " industry " means people at work and no amount of mechanization will make that statement false.

It is a discouraging fact that, in spite of all the advances in all branches of medical science, the general healthiness of mind and body of the community makes little or no progress. As sanatoria empty, mental hospitals fill; as nutritional defects diminish, cancers increase; as industrial poisonings become less frequent, stress diseases, mental and physical, multiply. Although it is generally accepted that the working hours have less to do with psychological trauma than the domestic ones, it is the claim of doctors who work in industry that by being known as part of the team they can exert a powerful influence for good on the positive aspects of the health of their companions, at all levels in the industrial structure.

This claim becomes nonsense if they are not accepted as part of the team. They cannot be so admitted unless they learn the facts of industrial life. There is a need for much work on the relevance of the arts of medicine to these problems and for pooling of experience, which alone can ensure that the same old errors are not endlessly and needlessly repeated.

The multiplication of casualty clearing stations, with a full complement of starch and chromium, will not denote the advance of occupational health, but an increasing tendency to bring trained doctors into consultation on many matters apparently far removed from the consulting room will. Those of us who hope for such an advance must do a great deal of fundamental preparatory thinking and research.

Summary

The attitude of an industrial medical officer to personal and general problems stemming from re-organization, redundancy, rehabilitation, and compensation inside industry is discussed. Some of the practical difficulties are illustrated and the view is expressed that only by becoming an integral advisory part of management can the doctor make his full contribution to the common good of all those working with him in the industry. The need for further studies of the impact of change and of the organization of internal rehabilitation and placement schemes, however primitive, is stressed.

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References

British Medical Association (1949). Duties of and Ethical Rules for Industrial Medical Officers.

Kennedy, A. (1957). *Lancet*, **1**, 261.

Stewart, Donald (1954). In *Industrial Medicine and Hygiene*, Vol. 1, p. 285, ed. Merewether, E. R. A. Butterworth, London.

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DERMATOSES IN THE MANUFACTURE OF GLASS FIBRE

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Continuous filament glass fibre is used in the manufacture of glass yarn and textile products. It is made from either alkali or alkali-free glass. The main ingredients of alkali glass are sand, lime, dolomite, and soda ash; for alkali-free glass no raw materials containing alkali are used, and boric acid is an additional major constituent. There are two methods of manufacture. (*a*) The glass is fed straight to the fibre-forming furnaces from a direct melt tank; or (*b*) it is made into solid glass marbles which are fed to the furnaces. The description which follows is confined to the manufacture of continuous filament by the latter process using alkali-free marbles.

Materials and Manufacture

The glass marbles are placed in hoppers from which they are mechanically fed to the furnaces. Each furnace consists of a sheet platinum crucible about 9 in. long, 5 in. wide, and 9 in. deep, with about 200 small holes in the bottom. The crucible is insulated by high temperature refractory material which leaves the bottom exposed; the crucible is electrically heated to about 1200° C. which melts the glass. The molten glass, under gravity, drips through the holes in the bottom of the crucible and is drawn into fine filaments by being wound on to a high-speed winder. As they are formed, the filaments are sprayed with a fine mist of cold water and then treated with an emulsion from a constant feed jet as they converge to a felt-covered pad to form a single multi-filament strand.

The furnace is situated about 12 feet above ground level, but only 5 feet above an intermediate platform on which the operator stands. This intermediate floor or platform communicates with the ground level by an opening through which the glass fibre passes to the collecting tube which is placed on the high-speed winding head.

The nature of the emulsion applied to the filaments at the pad level varies according to the use to which the glass fibre is to be put.

Glass fibre for textile use is treated with an emulsion which forms a protective coating against abrasion and fracture during the twisting and doubling of the fibre in the course of processing. This emulsion, which is slightly acid (*p*H 5·7-6·5) is applied at temperatures between 110° F. and 130° F., and contains the following ingredients:—

Dextrin Gelatine Polyvinyl alcohol	coating agents
Borax	buffer for *p*H
Hydrogenated vegetable oil	lubricant
" Athrol " (a polyethylene glycol oleate)	emulsifying agent
" Cirrasol " (fatty acid amide)	cationic agent for penetration and softening
Formaldehyde	antiseptic, anti-fungus

Glass fibre for the reinforcement of plastics is treated with an emulsion which will impart a protective coating and at the same time be suitable for further linking with phenolic and polyester resins and other media used in plastics. This compatibility is achieved by the addition of a " keying agent " to the emulsion. There are several varieties of emulsions, but the main ingredients are as follows:—

Polyvinyl acetate	coating agent
Di-butyl-phthalate	plasticiser
" Cirrasol "	cationic agent and softener
" Vitrafix ", a solution of methacrylato-chromic chloride in an isopropyl/acetone/water solvent	
V.T.C.S.	vinyl trichlorosilane

This type of emulsion is applied cold at a temperature between 60° F. and 75° F.

Environmental Conditions and Hazards

Glass fibre manufacture is hot and wet, and the operators are exposed to a relatively humid atmo-

FIG. 1.—Operator in glass fibre manufacture.

sphere. The room temperature varies from 80° F. to 90° F., and the relative humidity from 60% to 70%.

Operating and winding are the two main occupations in the manufacture of glass fibre. The work of the operator is illustrated in Fig. 1. He is in charge of a battery of furnaces and attends to faults in the glass as it issues from the crucible, and to breakages in the filament. In the course of his work, his hands are exposed to the radiant heat from the base of the crucible and to burns from molten glass. He has to handle the relatively coarse fibres issuing from the crucible and is liable to puncture wounds of the hands and feet. His hands are also exposed to constant wetting from water and emulsion. The work of the winder who attends to the winding machine is illustrated in Fig. 2. He is not exposed to the radiant heat hazard of the operator, but he is exposed to the other hazards of the operator and more so to the water and emulsion which come off the water guard and emulsion pad to fall to ground level.

The other workers are floaters, who relieve the operators and winders as required, graders and checkers, who test the fibres for quality, and cleaners, who clean the working area other than the actual machines which are the responsibility of the operators and winders.

Skin Lesions

The nature of the substance being converted into fibre and the various agents applied to it in processing, together with the hot, humid and wet conditions in which the process is carried on, are such that the various operatives consider that dermatological risks are to be expected in this employment. As a result of this belief, they only seek treatment when they have an established dermatitis. In such cases it is often impossible to determine whether the skin condition is occupational or not.

It was observed by one of us (D. A. M.) that paronychia and abnormal nail formation of the fingers commonly occurred among the employees in the continuous filament department. It was

thought that the condition might be due to a fungus infection of the skin and nails. All the employees in this department, a total of 126 males (60 winders, 51 operators, 13 checkers, one cleaner, and one fitter), were therefore asked to submit to a skin inspection, and all did so. It was found that in 63 (50%) the skin of the toes in the fourth interdigital space was peeling, and that eight operators had paronychia and abnormal nail formation of the fingers. These findings were suggestive of a fungus infection, and as the conditions at work were conducive to spread of such infection, it was considered that the problem was one for the attention of a dermatologist with experience of conditions in industry.

Investigation

At the request of the management concerned, arrangements were therefore made to carry out a further dermatological survey of the 126 operatives in the continuous filament department. Particular attention was paid to feet, hands, and nails, and where there was clinical evidence suggestive of fungus infection, scrapings were taken for mycological investigation.

The findings are summarized in the table. Three distinct clinical conditions were observed: paronychia, a "follicular eruption", and interdigital

TABLE

RESULTS OF DERMATOLOGICAL SURVEY OF 126 EMPLOYEES IN CONTINUOUS FILAMENT DEPARTMENT

	Fitters	Operators	Winders	Checkers
Paronychia	—	5	3	—
Maceration	1	25	32	5
Folliculitis	—	2	12	—
No. of employees ..	1	51	60	13

One cleaner had no abnormality of the skin

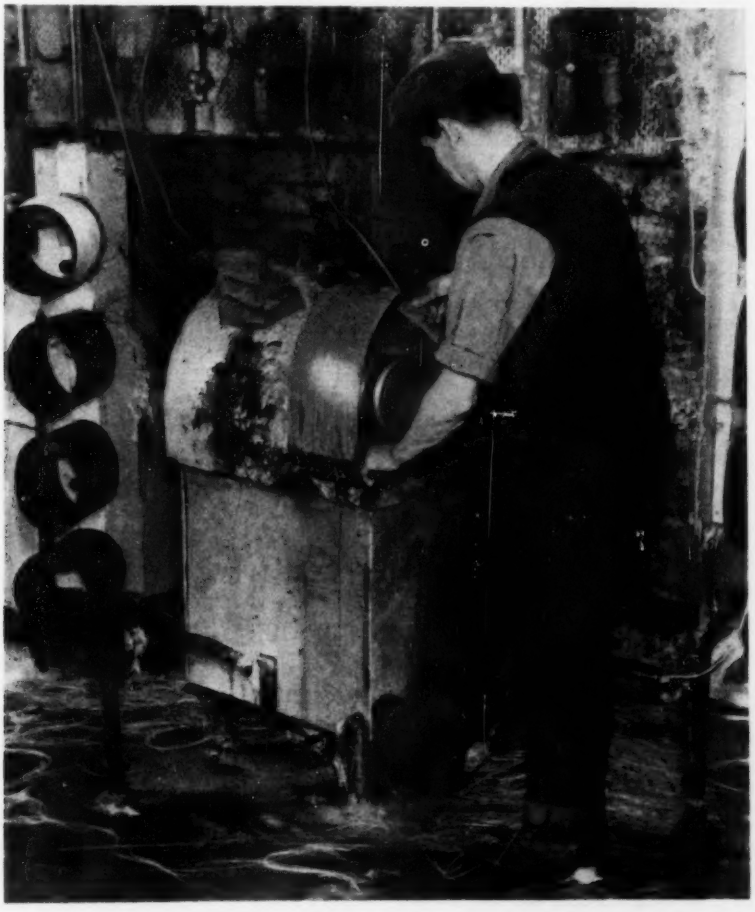

FIG. 2.—Winder in glass fibre manufacture.

maceration of the feet. Each will be described separately.

Paronychia.—Out of 126 operatives examined, eight cases (6·3%) of paronychia were observed. This condition involved the nail folds of one or more fingers, except in one case where the nail fold of the left great toe was affected, the inflammatory reaction being of a specific type. The nail fold was firm or indurated with minimal erythema and without the " bolstering " typical of pyogenic or yeast organism infections (Fig. 3). Tenderness was not a clinical feature and in only one case was there a history of pus formation. Secondary malformation of the nail was present in all eight cases, and in one onychorrhexis was complete. In spite of the clinical evidence of a low-grade inflammatory process the operative was not incapacitated. Direct and cultural mycological investigation in each case failed to reveal any specific pathogen. In three cases there was radiological evidence of glass spicules lying close to the nail fold in a site where clinical activity was at its maximum.

Folliculitis.—In 14 operatives (11·1%), we observed a fairly characteristic eruption involving the dorsum of the feet, lower third of the legs, forearms, and occasionally of the hands (Fig. 4). The lesions were in the main follicular in character, papular or papulo-pustular, not itchy, and dull red. In " susceptible " individuals the dermatosis was characterized by a period of exacerbation and complete remission unrelated to periods of work or holidays. Spontaneous involution occurred in all cases after a variable period. This eruption closely resembled the clinical picture of oil folliculitis observed in the engineering industry, and we suggest that this follicular reaction may have been produced by the hydrogenated vegetable oils and organic chemicals in the emulsion acting as follicular irritants.

FIG. 3.—The inflammatory reaction of the nail folds with secondary nail malformation.

FIG. 4.—Marked follicular papulo-pustulation of the forearms.

Interdigital Maceration of the Feet.—Out of 126 operatives examined, 63 (50%) revealed maceration of the interdigital clefts, the intensity of the reaction varying from a slight pallor to a complete denudation of the adjacent epidermal surfaces. The average case within this group exhibited, in addition to maceration, a variable degree of hyperidrosis and bromidrosis. Scrapings from the interdigital clefts of the 63 affected operatives were examined both microscopically and culturally and in only two cases was a specific pathogen found. This was *Trichophyton rubrum* in both cases.

The prevention of interdigital maceration constitutes a problem amongst operatives working under difficult atmospheric conditions. Clogs, loose-fitting footwear, and foot baths containing " penotrane " (Ward, Blenkisop & Co.) have been tried with little success, although the latter did reduce the incidence of bromidrosis. Other methods of dealing with this problem are at present being investigated.

Discussion

Siebert (1942), in an investigation of the possible industrial hazards in the manufacture of fibre glass, observed a mild irritative eruption, which disappeared within a few days, of the hands and forearms of new employees. Apart from this transient dermatosis, he failed to find any reference to any other new or unusual hazard in an exhaustive survey of the literature. These findings were confirmed by Sulzberger and Baer (1942), who considered that there was no direct evidence of sensitization and that the glass spicules were only superficially embedded. Schwartz and Botvinick (1943), although agreeing with the clinical findings, considered that sensitization could occur, not to the glass fibre but to the liquid binder, and that a degree of sensitivity developed in a considerable number of operatives. In this present survey no example of this transient irritation due either to mechanical causes or to contact with resin was noted, nor would such irritation have been expected as there were no new employees during the period of observation. Its occurrence was well known, and before the survey had been observed amongst new employees by one of us (D. A. M.).

A survey of the literature failed to reveal any reference to paronychia, a follicular eruption, or interdigital maceration of the feet, and we are of the opinion that the incidence is such as to warrant comment.

In view of the high incidence of maceration and associated hyperidrosis and bromidrosis, we expected there to be a correspondingly high incidence of tinea pedis, but this was not substantiated. In an attempt to determine the possible causative factors producing maceration, the type of footwear worn by the employees was examined. It was noted that maceration was present in 34% of those wearing wooden clogs and in 57% of those wearing leather boots or shoes. Examination of the leather footwear revealed a fine tenacious coating of resin and fibreglass sufficient to counteract the porosity of the leather. This purely mechanical occlusion in association with the warm atmosphere of work would in itself produce ideal conditions for the production of hyperidrosis and maceration from sweat retention. Although ventilation in clogs is minimal, they fit loosely and allow a steady flow of air over the feet.

The paronychia is, we suggest, directly associated with the implantation of glass splinters, which penetrate the skin in the region of the nail fold or pass between the nail fold and the nail, producing in both instances a foreign-body reaction. In three cases radiological evidence confirmed this hypothesis, which might well have been the cause in the remainder, the glass spicules having either been removed by the operator or worked themselves to the surface. The prevention of this condition is a most difficult problem, as the transparent and delicate nature of the glass filaments makes their removal a most difficult and intricate minor operation, yet this, in our opinion, is the only satisfactory solution. Consideration was given to the possibility of colouring the glass to facilitate its removal by the operative or industrial nurse, but this presented insurmountable technical difficulties. The use of industrial gloves fine enough to allow delicate movements was investigated, but again the combination of fibreglass and resin results in a markedly adhesive surface on the gloves. We consider that the immediate removal of the spicules by a trained and experienced nurse goes a long way towards reducing the incidence of paronychia.

Although the incidence of cutaneous lesions (69%) may seem unduly high, it is pointed out that of the three clinical conditions noted in the survey only paronychia could be of such severity as to incapacitate the worker. Although their incidence was high the operatives paid little or no attention to their presence and seemed to accept them as a natural consequence of this type of work.

Summary

The manufacture of continuous filament glass fibre is described. A dermatological survey of 126 operatives was undertaken. A clinical assessment of the skin conditions observed in these operatives is given with special reference to paronychia of the fingers (eight cases), folliculitis of the feet, legs, forearms, and occasionally of the hands (14 cases), and maceration of the interdigital clefts of the toes (63 cases).

In view of the high incidence of maceration, a correspondingly high incidence of tinea pedis was expected, but not found; in only two of the 63 affected cases was fungus (*Trichophyton rubrum*) demonstrated.

Radiological evidence in three cases confirmed our view that paronychia is due to glass spicules in the nail fold.

We are greatly indebted to Mr. R. C. B. Anderson, manager of the Glasgow Division of Fibreglass Ltd., and his staff for their wholehearted cooperation in this investigation. We would also like to express our thanks to Dr. James Somerville, Department of Dermatology, Western Infirmary, Glasgow, for his advice and helpful criticism.

References

Schwartz, L., and Botvinick, I. (1943). *Industr. Med.*, **12**, 142.
Siebert, W. J. (1942). *Ibid.*, **11**, 6.
Sulzberger, M. B., and Baer, R. L. (1942). *Ibid.*, **11**, 482.

Brit. J. industr. Med., 1958, **15**, 52.

ABSENCE FROM WORK IN RELATION TO WAGE LEVEL AND FAMILY RESPONSIBILITY

BY

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This paper discusses the relation between absence from work and wage level and absence and the number of dependants. The extent of overtime working is also considered. The investigation was made in a large iron and steel works.

Description of Firm

The plant is modern and the various processes of preparing the iron ores through to steel rolling are highly mechanized. There is a considerable diversity of occupations and physical conditions of work with few men employed on any one operation. Owing to the processes involved most production men are on continuous three-shift work, the plant being manned 24 hours a day throughout the year. The remainder of the men are mainly on discontinuous three-shift systems, work stopping over the whole or part of the weekend.

The majority of jobs in a section are arranged in promotion grades with corresponding differences in basic pay. In addition to the basic rate, men on production work receive a bonus dependent upon the output of their own or an associated section. Since the productivity of a department is largely determined by the capacity of the plant, skilful maintenance, and the supply of materials, this bonus is often relatively remote from individual effort and may be considered as part of a fixed wage. As well as the various wage levels within a department there are also differences in wage level between departments which have developed over the years. Thus jobs at the same wage level do not necessarily require the same skill and responsibility.

Other factors relevant to the study are the existence of a comprehensive medical service with two full-time medical officers and a staff of qualified nurses, and an employees' benevolent scheme which provides just over £1 per week after 14 days' sickness absence. There was a labour shortage in the works during the period studied. The absence rate was about 4% at which level the management did not consider absence to be a problem.

Sources of Data and Sampling Methods

The firm's individual absence records were compiled from clock cards and foremen's lists. The record distinguished between certified and uncertified sickness absence, absences with and without permission, and those due to injury. In many cases, however, it was difficult to establish the cause of absence and any classification must be treated with caution. The personnel cards were arranged by department and occupation and from these every fourth man was selected; in addition, data were extracted for men on the main production jobs, in all, approximately 1,000 men. For each man a note was made of his occupation, age, income tax code number, length of service, basic and bonus rate, annual gross earnings, absence during 1951-52, and number of hours paid. No cumulative record of actual hours worked, or of overtime, was kept. It was possible, however, to estimate the number of overtime hours paid for each man for a nine months' period.

Some indication of the physical demands and conditions of work—heaviness, temperature, continuity of working, etc.—was obtained from ratings by foremen and managers. Heaviness was rated from 1 for very heavy work to 7 for very light work, and temperature of the work situation as 1, 2, and 3 for hot conditions, some heat, and normal respectively. For further discussion of the procedure see Shepherd and Walker (1957). Ratings on most jobs were made by more than one person and the agreement between judges was found to be high.

Method of Analysis

For present purposes only those men on production jobs, on three-shift work (21 and 19 shift cycles), and employed throughout 1952 have been included.

They were from several departments but had similar hours of work which averaged 48 per week throughout all but a short part of the period.

The men were divided into six groups according to their hourly wage rate throughout 1952. This rate is independent of absence and overtime working and represents the pay associated with attendance during normal working hours. The pay intervals were arranged to provide approximately equal numbers in the groups, which were then divided into five on the basis of the income tax code number; these subgroups represented men with different numbers of dependants.* At this stage it was found necessary to exclude all men with no dependants owing to their small numbers in the higher pay groups. Men in the six wage groups were then matched as nearly as possible for income tax code number, age, heaviness of work, and temperature. Although this procedure reduced the number of men available from approximately 600 to 245, it was necessary in order to control important variables other than those under consideration. Table 1 shows that the wage groups were well matched for number of dependants and were reasonably comparable for age, heaviness of work, and temperature. The wage rate of the highest paid group was nearly double that of the lowest; when the average annual gross earnings were examined the difference in earnings between the extreme wage groups was about £300.

*The income tax code number has been used to give some indication of a man's family responsibilities. For further discussion see later.

Results

Absence and Wage Level.—Table 2 shows the total absence and the absence within each category for the six wage groups in terms of the number of absences and shifts lost. The figures given are rates which express the amount of absence per 100 men per year. Absences recorded as due to sickness but for which no certificate was brought were few and have been grouped with the certified sickness. The number of absences due to injury was very small and the figures are given only for the three lower and upper pay groups combined.

The total absence figures show that, apart from the lowest paid group, both the average number of absences and shifts lost increase as rate of pay increases. The relatively high absence of the lowest paid group is due mainly to more absences without permission and more longer absences with permission. In general absence without permission varies with wage level, although the association appears to break down in the highest and lowest wage groups. For absence with permission there is little relationship although, taken together, there is slightly more in the three lower pay groups. For sickness absence, however, there is an increase, both in shifts lost and number of absences, with increasing wage level.

TABLE 1

NUMBER OF MEN AT EACH WAGE LEVEL AND DISTRIBUTION BY INCOME TAX CODE NUMBER, AVERAGE AGE, AND AVERAGE RATING OF PHYSICAL CONDITIONS OF WORK

Hourly Rate (shillings)	No. of Men in each Income Tax Code Number Group				Total No. of Men	Average Age	Average Heaviness Rating	Average Temperature Rating
	50–89	90–109	110–124	Over 124				
3·4–4·09	9	8	9	9	35	43	4·3	1·6
4·1–4·29	12	12	12	12	48	42	4·1	2·1
4·3–4·49	12	12	12	12	48	42	4·1	2·2
4·5–4·89	9	10	10	9	38	43	4·2	2·2
4·9–5·99	10	10	10	10	40	40	3·8	1·9
6·0 and over	9	9	9	9	36	42	4·1	2·2
Total	61	61	62	61	245			

TABLE 2

AVERAGE NUMBER OF ABSENCES AND AVERAGE SHIFTS LOST PER 100 MEN PER YEAR, DURING 1952, FOR EACH CATEGORY OF ABSENCE

Hourly Rate (shillings)	Certificated and Uncertificated Sickness		Without Permission		With Permission		Injury		Total	
	No. Absences	Shifts Lost	No. Absences	Shifts Lost	No. Absences	Shifts Lost	No. Absences	Shifts Lost	No. Absences	Shifts Lost
3·4–4·09	14	206	340	488	46	257			403	1,117
4·1–4·29	13	169	216	260	35	98	5·3	109	271	602
4·3–4·49	27	333	231	325	46	92			310	850
4·5–4·89	34	487	305	366	29	76			374	1,087
4·9–5·99	43	810	358	428	25	55	3·5	94	425	1,293
6·0 and over	53	969	331	363	47	150			436	1,614

Thus the increase in total shifts lost at higher wage levels is due chiefly to the increase in recorded sickness absence while the greater total number of absences is the result mainly of more absences without permission.

The association between wage level and sickness absence is very marked; its explanation, however, raises a number of problems. For example, does the association indicate that there is more illness among men at higher wage levels ? To assist the discussion of this problem it was decided to tabulate the medical category for each sickness absence, to calculate the absence for the previous year, 1951, and to examine the number of absences of different lengths in each wage group, taking all absences into account.

In January, 1951, there was a widespread influenza epidemic. If equal exposure to infection is assumed it is of interest to compare the incidence of influenza at higher and lower wage levels. All but 14 of the men had been employed on the same occupation throughout 1951. Thus the wage groups were reasonably comparable during that period. On average there were seven cases of influenza per 100 men in 1951 and less than 1 per 100 in 1952. Of the 1951 cases, 75% were in the three lower wage groups with the lowest paid group having most of all. Also the average length of absence was slightly greater in these groups. While it is not known how much reliance can be placed upon the diagnoses, these figures suggest that men in the lower pay groups were more susceptible to infection.

The number of absences was mostly too small to allow any analysis by separate medical categories but on examination there was nothing to suggest that the number of more serious illnesses was greater in the upper wage groups. In 1951 the association between sickness absence and wage level was present but was less marked than in 1952. For the two-year period as a whole the time lost through sickness absence was about three times greater in the highest as compared with the lowest paid group.

Further evidence is obtained by taking all absence and examining the number and relative frequency of absences of different duration or length. In most cases it is difficult to obtain the true reason for an absence, or indeed any reason from the absence record, but the length of an absence provides some guide as to its cause, at least in general terms. For instance, of all single shift absences, 90% were " without permission ". (This kind of absence accounted for over 70% of all absences.) The remaining 10% were mostly " with permission ". For absences of over three shifts' duration, 60% were recorded as due to sickness or injury, 21% as with permission, and only 19% as without permission. Taking absences of over seven shifts in length, 90% were recorded as due to sickness or injury. This suggests that as the length of an absence increases beyond one shift there is a sharply increasing probability that the reason for it is either sickness (or injury) or one that would be accepted by management.

Table 3 shows the average number and percentage of all absences of given lengths for the wage groups and also, for comparison, the number recorded as due to sickness. For clarity the remaining wage groups have been reduced to two, but in view of its higher absence the figures for the lowest paid group are shown separately.

TABLE 3

(*a*) AVERAGE NUMBER OF ABSENCES OF EACH LENGTH PER 100 MEN IN 1952 AND (*b*) THEIR PROPORTION OF THE TOTAL NUMBER OF ABSENCES IN THE WAGE GROUP

Hourly Rate (shillings)	Length of Absence in Shifts						Total	Sickness Absences
	1	2	3	4-9	10-19	20 and Over		
(*a*) *Average number of absences per 100 men per year*								
3·4–4·09	266	63	3	57	8	6	403	14
4·1–4·49	218	25	7	29	5	6	290	20
4·5 and over	320	22	17	21	17	14	411	43
(*b*) *Table of percentages*								
3·4–4·09	66·0	15·6	0·8	14·1	2·0	1·5	100	3·5
4·1–4·49	75·2	8·6	2·4	10·0	1·7	2·1	100	6·9
4·5 and over	77·9	5·4	4·1	5·1	4·1	3·4	100	10·5

The table includes all absence, also the average number of absences per 100 men recorded as due to sickness for the same period.

The main differences between the middle and upper wage levels are (i) the number of single shift absences, (ii) the number of long absences (10 shifts and over), and (iii) the distribution by length of absences of two to nine shifts' duration, although the total number is approximately the same.

Although the number of wage levels is reduced in the table, further analysis showed that, apart from the lowest paid group, the number of single shift absences increased steadily as wage level increased.

A comparison of the distribution of lengths of absences in the middle and upper wage groups shows that the two distributions are quite different. In Table 3(*b*) the proportion of all absences of over one shift is much the same at both wage levels, *i.e.* 25 and 22%, but while the proportion of two and four to nine shift absences is greater in the lower paid groups there is a greater proportion of three and over nine shift absences in the upper wage groups. These trends are sustained in the lowest paid group. To some extent the changes in trend and distribution appear to be due to the National Insurance regula-

tions regarding sickness benefit*, but they also suggest that men at higher wage levels tend to take a longer absence for any given illness.

The number of sickness absences in the upper wage groups is twice as great as in the middle, and three times greater than in the lower wage group. These differences are partly associated with the number of long absences but not with corresponding differences in the number of absences of medium length, although many absences in this range are usually due to illness. To clarify the results all absences were tabulated by length and within each length by category, for the three wage groups. Nearly all absences of over nine shifts' duration were recorded as due to sickness or injury and the remainder as with permission. For absences of one to three shifts there was much more absence without permission at higher wage levels and less sickness absence and absence with permission. The most striking differences, however, were found in the absences of four to nine shifts. The figures are shown in Table 4.

TABLE 4

THE AVERAGE NUMBER AND PROPORTION OF FOUR TO NINE SHIFT ABSENCES IN EACH CATEGORY

Hourly Rate (shillings)		Sickness and Injury	With Permission	Without Permission	Total
3·4-4·09	No. Absences	9	31	17	57
	%	(16)	(54)	(30)	(100)
4·1-4·49	No. Absences	7	11	11	29
	%	(24)	(38)	(38)	(100)
4·5 and over	No. Absences	14	5	2	21
	%	(67)	(24)	(9)	(100)

The number of absences of four to nine shifts decreases with increasing wage level from 57 to 21 but the proportion recorded as due to sickness increases from 16% to 67%. Thus for absences of similar length men at higher wage levels brought sickness certificates to work more often than those at lower pay levels, although it is difficult to see why this should be so. It may be noted that most absences of four to nine shifts were recorded either as sickness or with permission and that while the absence in one category increased, that in the other decreased with wage level. Since the tendency to report illness, bring certificates, or seek permission for absence appears to vary with wage level, these results suggest that in some cases it may be more instructive to analyse the total absence in terms of the length rather than the category of each absence, and that comparisons of sickness absence figures alone may prove misleading.

The relatively higher absence of the lowest paid group is of some interest although the reasons for it are unknown. Later it will be shown that this group works more overtime than any other and there may be some connexion between this and the greater number of single shift absences. Tables 2, 3, and 4 show that this group has many more two-shift absences without permission and absences of four to nine shifts both with, and without permission, and it is these absences which chiefly account for the greater total shifts lost. In view of the tendency of the lower paid men not to report illness or bring certificates, it seems probable that these absences were mainly due to illness.

To summarize, men at higher wage levels lost more time through absence both in terms of shifts lost and number of absences. The greater shifts lost were mainly due to more long absences (10 shifts and over) in the sickness category while the greater number of absences was the result of more single-shift absence without permission. For absences of intermediate length (two to nine shifts) there was no increase with wage level, although their distribution by length varied, and the proportion of absences of four to nine shifts recorded as due to sickness was greater in the higher wage groups. On the question of whether men at higher wage levels experienced more illness, the available evidence was as follows: they did not have a greater number of more serious illnesses than those in lower pay groups; during an influenza epidemic they appeared least affected; they went absent more readily and appeared to take longer absences; lastly, they tended to report and bring evidence of illness more often. Further comment is left for the discussion.

Absence and Family Responsibilities.—Reliable information about marital status and number and age of children is difficult to obtain. In this study note was made of marital status from the firm's personnel card, and also of the man's income tax code number for the tax year 1952-53. The code number provides a reasonable index of marital status and number of dependants if the following assumptions can be made.* (i) That the code number

*" Benefit is payable only for days of incapacity which are part of a period of interruption of employment. Any two or more days of incapacity which occur within a period of six consecutive days, excluding Sundays, form a period of interruption of employment. Any two such periods of two or more days each, which are not separated by more than 13 weeks, are treated for benefit purposes as forming a single period of interruption of employment. Benefit is not payable for an isolated day of incapacity which does not form part of a period of interruption of employment. Sickness benefit cannot be paid for the first three days of a period of interruption of employment unless and until there have been at least 12 days of interruption of employment within the 13 weeks beginning on the first waiting day."

(Ministry of Pensions and National Insurance, Leaflet N.I.16.)

*The code number is only affected by children who are financially dependent on the parent; the family, however, may include other children now at work. A wife's earnings do not normally affect the husband's code number.

has not been " adjusted " in order to compensate for over or under deduction in the previous year. Errors of this kind should be randomly distributed over the population. (ii) That the man has no appreciable taxable private income or special allowances other than those for a wife and dependent children. This should be true for the majority. (iii) That the man's circumstances do not change throughout the period. This assumption clearly cannot be made for all men although it may be true for a considerable proportion of them providing the period is not greater than a year. Owing to the information available the groups used in this analysis are subject to any errors involved in making these assumptions. Table 5 shows the code number groups, the number of men, and their average age.

TABLE 5

INCOME TAX CODE NUMBER GROUPS, NUMBER OF MEN, AND THEIR AVERAGE AGE

Income Tax Code Number	Probable Family Responsibilities	No. of Men	Average Age
0–49	No dependants "Single "	22	37
50–89	One dependant " Married "	61	45
90–109	Two dependants " Married, 1 dependent child "	61	43
110–124	Three dependants "Married, 2 dependent children"	62	39
Over 124	Four or more dependants "Married, 3 or more dependent children "	61	41

Apart from the single men those included here are the same as those in the previous section. Individual code numbers were not available for the 1951-52 tax year. The code number intervals were defined after reference both to the marriage and children's allowances deductable in the tax year 1952-53 and to the distribution of code numbers for several hundred men. The code number intervals are sufficiently broad to allow for most of the variation in code number due to possible adjustments and allowances mentioned under (i) and (ii) above.

Groups of men at the same wage level within a works tend to have the same range of jobs and the conditions of work, and many other factors associated with any one occupation tend therefore to be equated between code number groups at the same pay level. As would be expected, however, there are differences in age distribution between the code number groups. There were few single men and the majority were comparatively young but some were in the very high age groups. Married men with no children also showed a bimodal age distribution, probably corresponding with those who were recently married, and those whose children were no longer financially dependent upon them. In this analysis no distinction between these two was made. In the higher code number groups the age distributions were restricted in range, unimodal, and had approximately the same means.

Table 6 shows the total absence figures of men with different numbers of dependants. The figures are shown for groups at different wage levels which, for greater reliability, have been reduced to two.

TABLE 6

AVERAGE NUMBER OF ABSENCES AND THE AVERAGE SHIFTS LOST PER 100 MEN DURING 1952 FOR MEN WITH DIFFERENT NUMBERS OF DEPENDANTS AND AT DIFFERENT WAGE LEVELS

Hourly Rate (shillings)		Income Tax Code Number				
		0–49	50–89	90–109	110–124	Over 124
		No Dependants	One Dependant	Two Dependants	Three Dependants	Four or More
3·4–4·49	No. absences	564	348	278	288	367
	Shifts lost	1,250	985	500	582	1,320
4·5–6·0 and over	No. absences	—	486	310	400	457
	Shifts lost	—	1,660	1,090	1,340	1,210
Total	No. absences	—	412	292	339	408
	Shifts lost	—	1,296	780	938	1,267

The relationship between absence and family responsibilities is U shaped. Absence is high for single men, falls to a minimum for men with two dependants, and then rises again. This is true for both pay groups although the level of absence differs. In general, it will be noted that the increase in absence at higher wage levels is present in all code number groups.

The higher absence of men with three or more dependants is of some interest, and the total absence was analysed first by the category and secondly by the duration or length of each absence. Table 7 shows the absence without permission and the sickness absence for the code number groups. Absence with permission has been omitted but it showed much the same relationship with family responsibilities, except that men with no dependants had very little absence in this category. Injuries appeared to follow the same U-shaped relationship, but their number was too small to allow any conclusion to be drawn.

It will be seen that in the case of absence without permission the U-shaped pattern of absence with family responsibilities is consistent at both pay levels. Also, as shown in the previous section, absence is greater at the higher pay level.

Sickness absence also follows the same U-shaped pattern in the lower pay group but is not quite as regular in the higher one. When the number of men having one or more sickness absences in the year was examined, however, the relationship was found in both pay groups.

TABLE 7

AVERAGE NUMBER OF ABSENCES AND SHIFTS LOST PER 100 MEN DURING 1952 IN SICKNESS AND WITHOUT PERMISSION FOR MEN WITH DIFFERENT NUMBERS OF DEPENDANTS AND AT DIFFERENT WAGE LEVELS

Hourly Rate (shillings)		Sickness Absence					Absence without Permission				
		Number of Dependants									
		None	One	Two	Three	Four or More	None	One	Two	Three	Four or More
3·4–4·49	No. absences	36	24	13	15	21	490	267	231	239	282
	Shifts lost	495	458	69	155	339	673	373	297	306	400
4·5–6·0 and over	No. absences	—	61	17	56	39	—	364	255	317	393
	Shifts lost	—	761	717	834	636	—	446	283	379	443
Total	No. absences	—	41	15	34	30	—	311	242	275	332
	Shifts lost	—	596	377	472	495	—	406	290	340	419

Table 8 shows the frequency of all absences of different lengths for each code number group for the total sample. Single men have been included but, as they were all at the three lower wage levels, their absence figures are not strictly comparable with other groups.

TABLE 8

AVERAGE NUMBER OF ABSENCES OF EACH LENGTH PER 100 MEN IN 1952

Length of Absence in Shifts	Income Tax Code Number				
	0–49	50–89	90–109	110–124	Over 124
	No Dependants	One Dependant	Two Dependants	Three Dependants	Four or More
1	418	295	223	261	310
2	73	38	33	21	24
3	14	10	6	11	16
4–9	41	44	20	23	31
10–19	14	12	5	13	15
20 shifts and over	4	13	5	10	12
Total	564	412	292	339	408

The table includes all absence.

The table shows that the U-shaped relationship is present in both the short absences, which are mainly without permission and in the longer absences which are chiefly due to illness.

The largest differences between groups are found in the number of single, and over-three shift absences, and the question arises whether the latter reflect genuine differences in the incidence and severity of illness. This point will be referred to in the discussion.

To ensure that the U-shaped absence pattern was not due to the age differences between the groups, a 10-year age group was examined. The men in this restricted age range were grouped by their code number and the groups were matched for wage level. The absence pattern both for shifts lost and number of absences was maintained and is therefore not due to age.*

Wage Level, Family Responsibilities, and Overtime Working.—No cumulative record of actual hours worked or of overtime was kept, only the number of hours paid was recorded. These took into account special shift and overtime allowances. Thus one hour's work paid at time and a half would be recorded as one and a half paid hours. It was possible, however, to estimate† the number of overtime paid hours for each man for a nine-month period and these were calculated for the men in each of the original 24 groups which divided the sample by wage level and family responsibilities. The overtime paid hours cannot be translated into actual hours, but they provide some indication of the relative amounts of overtime worked.

On three-shift systems there are few occasions on which overtime work is possible and it occurred mainly on rest days or, occasionally, when two consecutive shifts were worked. From the records available it was impossible to discover whether opportunity for overtime was similar in different occupations. At any one wage level, however, men are mostly on the same range of jobs and should have equal opportunities for overtime working. It is therefore possible to compare the overtime of men with different numbers of dependants who are at the same wage level. Opportunity may not have been comparable, however, at different wage levels.

The results are shown in Fig. 1. For greater reliability the upper four wage groups have been reduced to two, but as the absence of the lowest

*As discussed above, age and family responsibilities are related, although the relation is complex. In view of the association between number of dependants and absence it is of interest to re-examine the relationship between age and absence, taking family responsibilities into account. This has been done by Dr. B. Petz but the results have not yet been published.

†Estimated overtime paid hours = (actual paid hours) plus (hours lost × C) minus (planned " paid " hours),

where $C = \frac{\text{Planned " paid " hours}}{\text{Planned hours}}$

paid group was not consistent with the general trend, the overtime figures are shown separately.

Fig. 1 shows that the relation between family responsibilities and the extent of overtime working depends upon wage level. At lower wage levels there is a considerable increase in overtime working with increasing family responsibilities. In the higher pay groups there is little or no relationship.

The variation in overtime working between different code number groups is as great as that between the wage levels. As wage level increases the extent of overtime working diminishes; this trend is sustained in all code number groups. It seems unlikely that these trends merely reflect differences in opportunity for overtime but the possibility remains.

There are two further points of interest. Although men with over three dependants have more absence they also work more overtime. Similarly, the lowest paid group has the highest overtime figures as well as a higher absence rate. Thus in these groups a higher absence rate does not necessarily indicate a lower overall attendance rate.

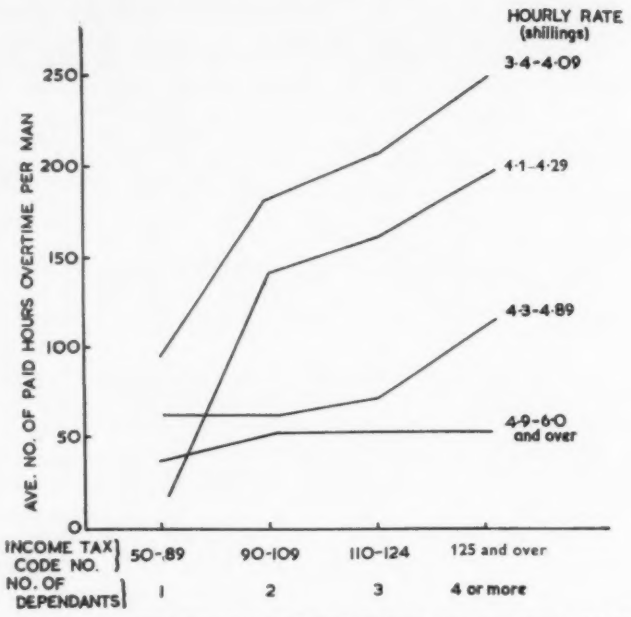

FIG. 1.—The average number of paid hours overtime per man from April to December, 1952, for groups with different numbers of dependants and at different wage levels.

In connexion with these results, two characteristics of income tax are relevant: (i) As taxable income increases the rate at which tax is levied increases by steps up to the standard rate. Thereafter the amount of tax increases as a simple function of income. Thus the value of an extra pound in wages, whether from overtime working or other source, decreases as income level increases. (ii) At a low rate of tax any allowance against taxable income is of less value than at a higher rate. Thus at lower gross income levels men with several dependants derive less benefit from their income-tax allowances. Thus for men at the same gross wage level and for the same attendance at work the difference in net income between men with one and four dependants respectively is small at low income levels but increases rapidly as wage level increases. Differences in income of similar magnitude appear to affect overtime working. The changing relation between overtime working and number of dependants as wage level changes may therefore be due partly to characteristics of income tax.

It is of interest to note that the actual difference in net income between those with one and four dependants was almost constant at all wage levels. (The actual differences were from the lowest to the highest wage levels £76, £76, £61, £72, £70, £87. For the same total attendance the expected differences would be £24, £35, £38, £47, £65 and £82.) This constancy results mainly from the lower absence and greater overtime working of men with several dependants at lower wage levels.

Discussion

Before discussing the findings some possible limitations must be considered. The results are based on data from one works and in an industry where there are wide pay differentials which are not always closely related to skill or responsibility. This situation is a favourable one for investigating the relation between wage level and absence but the results may not be applicable to situations where pay and responsibility are closely linked. This qualification should not apply to the results relating to family responsibilities. It should also be remembered that the findings concern men on three-shift work.

At lower pay levels overtime working increased markedly in groups with progressively greater family responsibilities: in the higher pay groups there was little or no relationship. One interpretation of this result is that the higher paid men with dependants, unlike those with a lower income, felt no need to supplement their earnings by working overtime. The result showing that as wage level

increased the extent of overtime working decreased must be treated with caution since opportunity may not have been comparable. There is no direct evidence that income tax or tax reliefs affected these results but they could partly account for the particular relationships found.

The association between sickness absence and wage level was very marked and the problem arises whether the greater absence reflects an increase in illness at higher wage levels. This raises the general question of the relation between illness and absence from work and between the incidence and severity of illness in a group and the amount of sickness absence. For the range of income under investigation, there appear to be no *a priori* grounds for suspecting a greater incidence of illness in the higher paid groups but the possibility cannot be ruled out. When comparing sickness absence rates, however, it is necessary to enquire whether any differences are attributable more to differences in the tendency to go absent when ill, report an illness, or bring a certificate on returning to work, than to differences in the amount of illness itself.

Analysis showed that at lower wage levels some absences of medium length which were probably due to illness were either not reported or recorded as such. In these groups there were few absences of three shifts but relatively many absences of four to nine shifts and it might be expected that the men would obtain sickness certificates and avail themselves of National Insurance benefit. Here it may be noted that the regulations are such that it is often necessary to obtain two certificates, or one and a note, if the man is both to claim benefit and bring evidence of illness. If he belongs to a private sick benefit club, a third certificate may be required. There was no paid sick leave scheme in the works and for short-term absence there was no great incentive, financial or otherwise, to bring a certificate. Thus whether one was brought may depend on many other factors beyond the scope of this study.

While no definite conclusion can be drawn it seems likely that the greater recorded sickness absence of the highest paid groups was attributable more to a change in the response to illness than to any differences in the incidence of illness itself. If this is correct the results showing an increase in absence at higher wage levels are best explained in terms of (*a*) a greater tendency to go absent for any given reason, illness or otherwise, (*b*) a tendency to stay away longer for any given illness, and (*c*) differences in the reporting of illness.

If the assumption of equal incidence and severity of illness is correct the question arises whether the greater total shifts lost at higher wage levels were in any sense unnecessary. In this works absence entailed a complete loss of wages and it might be argued that the sickness absences of all men, including the higher paid, were mainly due to their feeling unfit for work. If this was so, it may be asked whether the lower paid men were remaining at, or returning to work when they were unfit to do so. The results suggesting that during the influenza epidemic of 1951 men in the lower wage groups were most affected may have some bearing on this question.

The results of this study also suggest that comparison of sickness or other absence rates may be misleading unless the distribution of wage rates and family responsibilities are fairly similar in the groups compared.

Previous work on the relation between wage level and absence is limited, although many authors mention the importance of pay. In 1928 Vernon and Bedford reported that the absence rate for colliers varied between 17·3% and 16% as the mean wage index varied from 163·1 to 147·5. In a later report (1931), the same investigators conclude that " absenteeism is greatly influenced by economic conditions, for when the possible earnings of coal-face workers fell by 32%, the time lost by voluntary absenteeism fell to a half, and that lost by sickness fell to three-fourths." Other underground and surface men also showed reductions. These results, however, must be treated with caution. The period covered by the study, 1924-28, was one of great upheaval in the industry and during this time, apart from the long dispute in 1926, the fall in possible earnings was associated with a reduction in the number of possible shifts per week.

Recent investigations (Buzzard and Shaw, 1952) and Denerley (1952) have shown that when a paid sick leave scheme is introduced the time lost through sickness is substantially increased. Although some abuse seems inevitable the writers consider it to be small in extent and suggest two ways in which the scheme may affect sickness absence. First, it " will enable many people to be absent who ought to have been absent before " (Buzzard and Shaw), and, second, it " may help to prevent further sickness by providing the opportunity to recuperate fully before resuming work " (Denerley). Buzzard and Shaw also report a " distinct and striking difference between workers who receive incentive payment and those who do not ". Not only the sickness rate but also the proportional increase after the introduction of the scheme was lower for the incentive worker. They note that this may in part be due to the fact that the incentive worker receives less money when absent sick than when at work. The day wage man on the other hand may actually be a little better off

when sick if possible overtime earnings are not considered.

These studies show that factors other than the incidence and severity of illness play an important part in determining the amount of sickness absence although the latter must clearly have some limiting effect. The evidence suggests that a man's willingness to go absent when ill, or return to work when on the way to recovery, is to a large extent a function of his financial circumstances before and during the absence.

In the present study the relationship between absence and family responsibilities was found to be U shaped. Absence was higher for single men, fell to a minimum for those with two dependants, and then increased progressively for men with more than two dependants. The U-shaped relationship between absence and number of dependants was found in all categories of absence including sickness absence. It was also found for absences of all lengths. Thus the extent of a man's family responsibilities affects his total absence behaviour rather than any particular category or length of absence.

Noland (1946) reported that those with the least absence had more dependants but he gave no details or figures. Whitehead (1948), in a study of Australian munition workers made during the war, found that

> " of female workers who had children, those with three or more children had the most absences and lost most time through sickness absence. Among male workers those with children, on average, had fewer absences and lost less time than those without children; however, among those with children the rates tended to increase with the number of children, although these variations were not statistically significant."

Comparing wage levels, there was no reason to expect differences in the incidence of illness but in comparing men with different numbers of dependants there are some *a priori* grounds for suspecting systematic differences in the amount of illness. Men with several dependants may experience a greater degree of stress of various kinds than those with few dependants. There may also be differences in the exposure to infection. It may be noted that men with several dependants had more sickness absence but also worked more overtime. This situation may be contrasted with that of men at higher wage levels who had more sickness absence but who worked less overtime. While great caution is necessary in interpreting differences in sickness absence figures the results are consistent with the view that differences in family responsibilities are associated with differences in the incidence of illness.

The underlying factors which give rise to the association between absence and number of dependants are complex and require further studies, probably of an interview nature. Among the many variables to be considered are differences in (i) financial status and security between groups due, for example, to income tax reliefs, family allowances, etc., or to differences in the number of wage earners per family unit; (ii) the care the individual receives when ill, which may also be determined by family composition, and (iii) the leisure habits and needs of men with differing family responsibilities.

The findings as a whole suggest that an absence from work may be considered as the result of a choice on the part of the individual. On most working days of the year the question of whether to attend or not may never arise. Three-quarters of the men had fewer than five absences a year. Thus the balance is normally weighted heavily in favour of attendance. In the case of many injuries and more serious illnesses absence is of course inevitable, but these, relative to other absence, are rare events. The problem of absence from work may therefore be conceived as that of discovering the main factors which singly or together determine whether and when this " choice " situation will occur and those which determine the outcome. For example, slight indisposition may be thought of as an event which precipitates a " choice " situation, while wage level or a paid sick leave scheme are factors which may partly determine the outcome. Thus two broad groups of causal factors may be distinguished: (*a*) the more immediate and often highly specific factors or events which raise the question of whether to go absent or not; and (*b*) the more long-term and general factors which determine how heavily weighted is the initial balance towards attendance. The latter implies the concept of an individual absence threshold, the level being determined by both personal factors and by the general conditions of work.

The specific events underlying an absence are usually commonplace and correspond most closely to a " reason " for it. However, events or potential " reasons " of one particular kind, or class, may occur more often in some groups than others, *e.g.*, in groups with differing family responsibilities; they may also be associated more with some times of the day,* or days of the week, than with others. One step towards understanding, predicting, and coping with absence lies in discovering such associations. Of the more general factors the problem is to find the most important in determining how strongly the individual will strive to maintain full attendance at work. The evidence in this paper suggests that

*In this connexion the authors found (1956) that on three-shift work, three-quarters of the single-shift absences without permission occurred on the morning (6 a.m. to 2 p.m.) shift, and appeared to be associated with the early start.

wage level may be one such factor. Family responsibilities may also act in this way but, in addition it seems likely that the question of whether to go absent or not occurs more frequently in some family responsibility groups than in others.

Summary

Men at different wage levels employed in an iron and steel works were compared with respect to their absence from work and overtime working. The men were also grouped according to their family responsibilities, or number of dependants, as indicated by their income-tax code number. There was no paid sick leave scheme.

The amount of overtime working decreased at higher wage levels. This trend was found in all family responsibility groups. There was a relationship between family responsibilities and overtime working but its nature depended upon the wage level of the men concerned. At lower pay levels overtime working increased markedly in groups with progressively greater family responsibilities; at higher pay levels there was little or no increase.

Men at higher wage levels lost more time through absence, both in terms of shifts lost and number of absences. The increase in total shifts lost was due mainly to more long absences (10 shifts and over) recorded as due to sickness, while the increase in the total number of absences was due chiefly to more single-shift absences recorded as without permission. For absences of intermediate length (two to nine shifts), there was no increase with wage level, although their distribution by length varied and the proportion recorded as due to sickness was greater in the higher wage groups.

The relationship between absence and family responsibilities was found to be U shaped. Absence was higher for single men, fell to a minimum for those with two dependants, and then increased progressively for men with more than two dependants. This result was independent of wage level and was found in all lengths and categories of absence including sickness absence.

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References

Buzzard, R. B., and Shaw, W. J. (1952). *Brit. J. industr. Med.*, **9**, 282.
Denerley, R. A. (1952). *Ibid.*, **9**, 275.
Noland, E. W. (1946). *Factory Management and Maintenance*, **104**, No. 1, 131.
Shepherd, R. D., and Walker, J. (1956). *Occup. Psychol.*, **30**, 105.
——, —— (1957). *Brit. J. industr. Med.*, **14**, 266.
Vernon, H. M., and Bedford, T. (1928). *Rep. industr. Fatigue Res. Bd. (Lond.)*, No. 51.
——, —— (1931). *Rep. industr. Hlth Res. Bd. (Lond.)*, No. 62.
Whitehead, M. (1948). Bull. industr. Psychol. Personnel Pract., **4**, No. 3, p. 3.

Brit. J. industr. Med., 1958, **15**, 62

STUDIES ON THE RISKS ASSOCIATED WITH THE USE OF PARATHION-IMPREGNATED GAUZE STRIPS IN FLY CONTROL

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Organic phosphorus compounds are being increasingly used as insecticides. They are the most effective of all substances tested and the tendency of insects to develop resistance to them appears to be very small in comparison with that developed to such insecticides as the halogenated hydrocarbons.

The main disadvantage of most organic phosphorus insecticides is their high toxicity for warm-blooded animals and human beings, whom they affect by inactivating the enzyme cholinesterase. Some of these substances seem, moreover, to be capable of inflicting nerve damage which may or may not be connected with the cholinesterase inactivation (Bidstrup, Bonnell, and Beckett, 1953; Barnes and Denz, 1953; Fenton, 1955; Durham, Gaines, and Hayes, 1956).

Organic phosphorus compounds are used as insecticides in agriculture and horticulture, and are applied as aerosols in order to produce a knock-down effect. Attempts have also been made to use the " systemic " effect of these compounds by causing them to be taken up into plants in order to destroy insects feeding thereon. Organic phosphorus compounds have also been applied as residual insecticides, for example, in fly control. Thus experiments have been made in placing parathion-impregnated gauze strips in stables and cowsheds, which proved remarkably effective (Wichmand, 1953; Glömme and Swensson, 1955). Parathion is diethyl-*para*-nitrophenylthiophosphate. Similar applications have been tested elsewhere (Maier and Mathis, 1955; Kilpatrick and Schoof, 1956). We have carried out a field investigation and laboratory experiments with animals in order to determine whether the last procedure may endanger the health of the workers.

The Impregnated Gauze Strips

The use of parathion-impregnated gauze strips under the roof in stables and cowsheds to combat flies was introduced in Denmark in 1952 (Wichmand, 1953). The flies, settling on the strips, come into direct contact with the parathion and rapidly die. As parathion evaporates very slowly, the insecticidal effect of the strips persists for at least five to six months. The method is effective and is widely used in the Scandinavian countries.

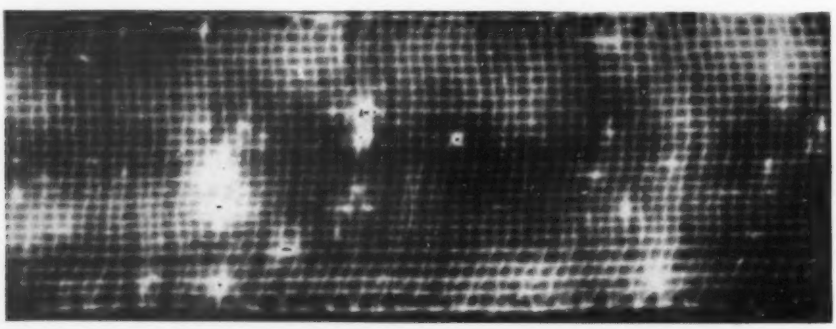


FIG. 1.—Autoradiogram of gauze strip impregnated in the usual way with parathion containing radioactive phosphorus.

The strips of gauze are soaked in a solution of technical parathion in such a way that every square metre contains about 3 g. of parathion. The technical product is not pure, but contains small quantities of certain other substances having a similar biological effect, *e.g.*, various S-isomers and paraoxon (where sulphur is replaced by oxygen) and the decomposition product p-nitrophenol, which has no effect on cholinesterase.

The distribution of the parathion is not uniform throughout the strip. Fig. 1 shows an autoradiogram of a strip which has been impregnated in the usual way with parathion containing radioactive phosphorus (P^{32}).

The strips are sold in hermetically sealed packets, and are placed under the roof in stables and cowsheds. On the packet there is a notice stating that protective gloves should be worn when mounting the strips, that the packet and any unused strips should be destroyed immediately after use, and that the strips are highly poisonous to animals and human beings. The strips must not be used in human habitations.

The manufacturers recommend the use of 1 square metre of the strips (containing about 3 g. of parathion) to every 30 square metres of roof surface.

The use of gauze strips is superior to the indiscriminate application of parathion powder on beams and window-sills.

Control Methods

As organic phosphorus insecticides inactivate cholinesterase (ChE) in warm-blooded animals and as this inactivation varies with the quantity of insecticide absorbed, it is possible to determine the degree of exposure by ascertaining the ChE activity in various tissues. For practical clinical work determination in blood is used.

Repeated exposure to and absorption of small quantities of the insecticide leads to a cumulative effect, as recovery of ChE after each exposure is slow, but variable.

Of the various methods which have been given for determining the ChE in blood, we used the gasometric technique in the modification described by Augustinsson (1948). In this method the acid formed in the enzyme reaction is taken up into a bicarbonate system, and an equivalent quantity of CO_2 is released and recorded as the volume of CO_2 (in μl) which is formed in 30 min.

It is assumed that there are two different groups of cholinesterases. One group, the acetylcholinesterases (AChE), are characterized by the fact that they break down acetylcholine more rapidly than other esters. Acetylcholinesterase occurs mainly in the erythrocytes and in the brain. The second group, the butyrylcholinesterases (BChE), are characterized by their capacity to break down butyrylcholin, BChE, which is thought to be formed in the liver, and occurs mainly in blood plasma. The BChE activity in the plasma is lowered in certain liver diseases. In the literature AChE is often called " true cholinesterase " and BChE " pseudocholinesterase ".

In our investigations we used acetyl-β-methylcholine in the substrate for determining AChE activity and butyrylcholine for determining BChE activity. The lowering of BChE activity in plasma generally occurs first and is strongest. The AChE activity of the erythrocytes is affected later and falls more slowly.

The method has been made more suitable for field investigations by a modification of the blood tests which has been worked out by Augustinsson and Heimbürger (1953).

Exactly 0·05 ml. of blood is taken up in a pipette and applied in a thin layer on filter paper.

The paper used is a filter paper in general laboratory use, Munktell No. 3. Other papers of good laboratory quality may be used as well, *e.g.*, the Whatman papers. The paper is allowed to dry in the air and is then mailed to the laboratory. If kept cool it can be preserved for several months without affecting the result of the analyses. In the laboratory the whole blood spot containing a known amount of blood (in the general procedure 0·05 ml.) is cut in small pieces with a pair of scissors and put directly into the main compartment of a Warburg flask. Ringer's bicarbonate solution is then added. The material is extracted for half an hour. This method has the advantage that the investigations can be centralized and the results are therefore more consistent and reliable.

Field Investigations

Before allowing the use of parathion-impregnated gauze strips in Sweden the authorities gave special permission for certain tests to be carried out. An investigation of a group of farm-workers employed in the cowsheds where the strips were being tested was therefore made in 1954.

For this investigation 43 cowsheds of different types and sizes in central Sweden were selected and the tests were undertaken during the months of May and June.

TABLE 1

NORMAL VALUES OF CHOLINESTERASE ACTIVITY IN BLOOD (AUGUSTINSSON, 1955) AND PRESENT FIELD INVESTIGATION USING THE SAME METHOD

	Cholinesterase Activity in Erythrocytes (AChE)			Cholinesterase Activity in Plasma (BChE)		
	Mean (μl CO_2/30 min.)	Standard Deviation	Number of Observations	Mean (μl CO_2/30 min.)	Standard Deviation	Number of Observations
From Augustinsson*	35·4	4·7	300	75·5	14·7	294
Initial value in field investigation	34·0	3·5	43	80·2	17·8	43

*Augustinsson's values are based on 300 and 294 estimations on samples from 141 and 116 individuals respectively.

The farmworkers concerned were examined before the strips were installed and again one week, and in some cases one month, after the strips had been applied. A general medical examination and determination of the ChE activity in the blood were undertaken.

In the general examination it emerged that some workers had felt ill or had had a headache after the application of the impregnated gauze strips. No objective signs and no diminution of BChE activity were, however, established.

Acetylcholinesterase and BChE activity show considerable variations between different individuals (Augustinsson, 1955). Augustinsson's results are given in Table 1 together with the absolute activity values for our group, consisting of male cowhands aged 17-65 years. In view of the considerable individual differences in cholinesterase activity it is preferable to use a determination made on the same individual as a baseline before exposure. Even with the same individual, however, there may be variations (Augustinsson, 1955) which must be taken into account when assessing isolated values.

TABLE 2

DETERMINATION OF CHOLINESTERASE ACTIVITY IN BLOOD OF EMPLOYEES WORKING IN LOCATIONS WHERE PARATHION-IMPREGNATED GAUZE STRIPS HAD BEEN APPLIED (MAY AND JUNE, 1954)

	Number of Employees Examined	Cholinesterase Activity as % Activity before Application of Strips	
		Erythrocytes (AChE)	Plasma (BChE)
Before application	43	100 ± 1·6	100 ± 3·5
One week after application	43	101 ± 1·4	100 ± 3·6
One month after application	12	99 ± 2·7	98 ± 4·0

In Table 2 the average values for the AChE and BChE activity have been expressed as a percentage of the value determined before application of the strips. The activity of ChE was not reduced during a period of one month after the strips had been applied. This is probably due to the insignificant evaporation of the parathion and to the fact that in the technical parathion used the content of related substances with greater volatility was small, and to the fact that the ventilation in the cowsheds was good, being estimated at an average of 10 to 20 air changes per hour.

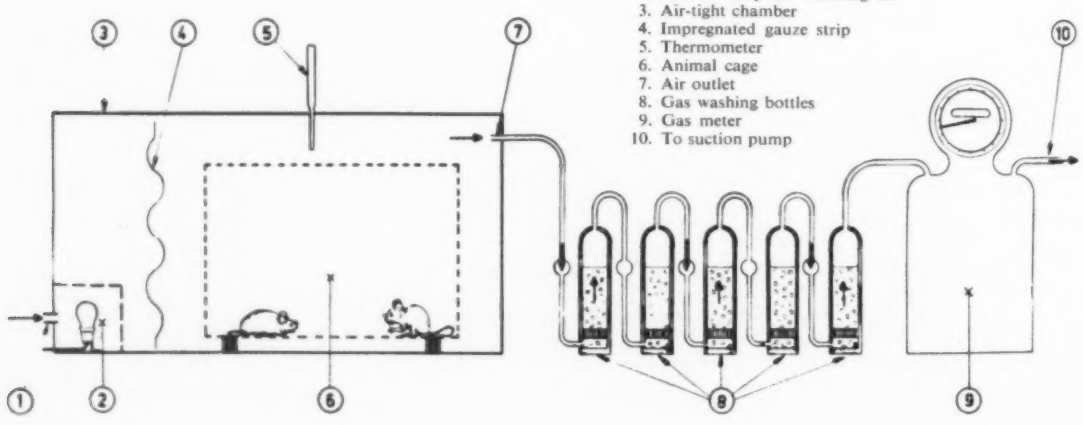
Experimental Investigations

For the experiments with animals guinea-pigs were used, in simple exposure chambers (Fig. 2), in which the temperature and ventilation could be varied. In these chambers were placed commercial parathion-impregnated gauze strips said to contain 3 g. of parathion per square metre. One-third of a square metre of impregnated gauze was used to every square metre of floor surface, *i.e.*, about 10 times as much as is recommended for combating flies in stables and cowsheds. The parathion content of the strips was estimated and found to vary from 2·5 to 3·1 g. per square metre. The ventilation was varied between 0·5 and 2·5 air changes per hour. The temperature in some experiments was maintained at 25 to 26° C. and in others at 30 to 32° C.

Attempts to determine the concentration of parathion in the exposure chamber by absorption in ethanol or caustic soda were unsuccessful.

Blood samples to determine ChE activity were taken by cardiac puncture without anaesthesia before the experiment, after three and seven days' exposure and, in some experiments, weekly up to six weeks' exposure. Usually only the BChE activity was determined, as this is high in guinea-

FIG. 2.—General arrangement of experiments.
1. Air inlet
2. Electric lamp for warming air
3. Air-tight chamber
4. Impregnated gauze strip
5. Thermometer
6. Animal cage
7. Air outlet
8. Gas washing bottles
9. Gas meter
10. To suction pump



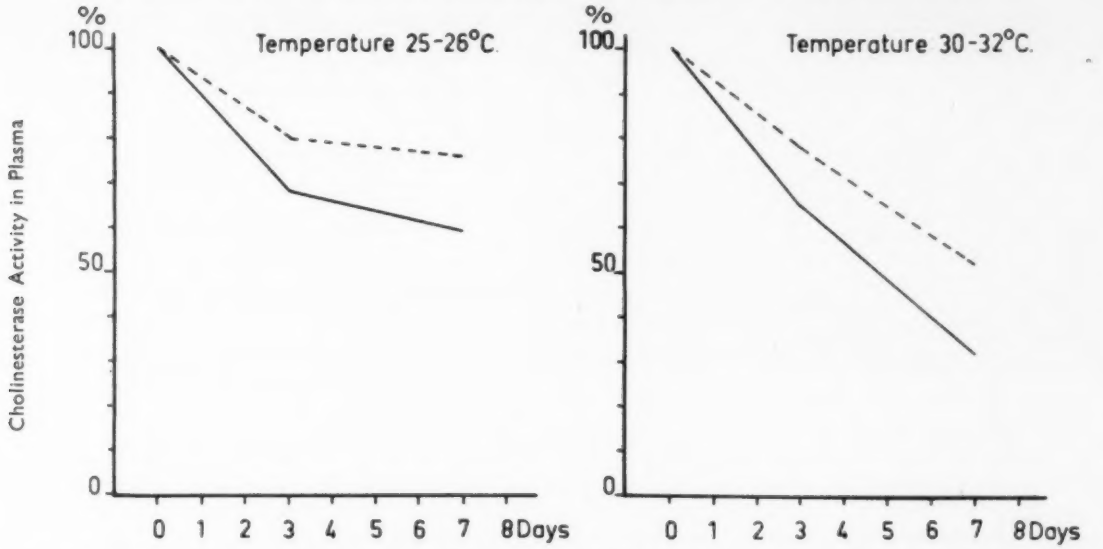


FIG. 3.—Effect on plasma cholinesterase activity (BChE) of continuous exposure in the experimental chamber at different temperatures and ventilations.

Solid line represents 0·5-1·2 air changes per hour, and dotted line 1·5-2·5 air changes per hour.

pigs. The AChE activity in the erythrocytes of guinea-pigs is low and the assessment of changes as a sign of exposure is therefore somewhat more uncertain. Both the experience of others and our own studies show that the effect of parathion on AChE and on BChE activity is essentially similar, but BChE activity reacts more quickly.

In guinea-pigs, as in human beings, considerable variations in BChE activity are found between different individuals. The mean activity (μl CO_2/30 min.) for a group of unexposed guinea-pigs (n = 156) was 73·3 $\pm$ 1·27 (σ = 15·8). The BChE activity of each exposed animal was recorded as a percentage of the activity before exposure.

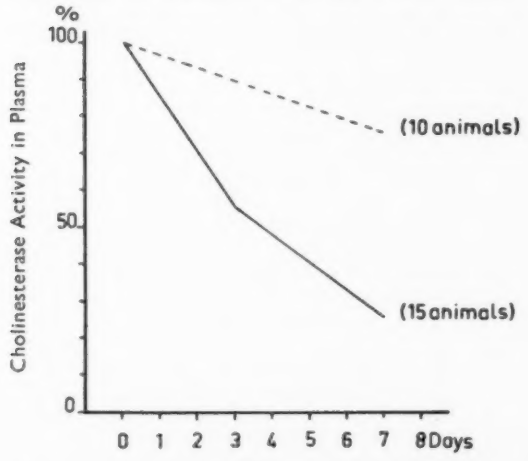


FIG. 4.—Effect on plasma cholinesterase activity (BChE) of exposure in the experimental chamber for eight hours a day and continuously at 30 to 32° C. and 1 to 1·2 air changes per hour.

Solid line denotes animals exposed continuously, and dotted line those exposed eight hours per day.

As will be seen from Fig. 3, the animals showed a decrease of BChE activity which was more marked both at the higher temperature and with reduced ventilation.

Continuous exposure was compared with exposure for eight hours a day. In the latter case, as might be expected, the effect on BChE activity was less (Fig. 4).

In a few experiments with prolonged exposure it was found that after one to two weeks—the time varying somewhat with different experimental conditions—BChE activity settled at a stable level (Fig. 5). The strip in the exposure chamber was changed every week. Further experiments, continued for six weeks, gave substantially the same results. Similar results with repeated exposure of rats to sarin, another organic phosphorus compound, were obtained by Cohen, Oberst, Crook, and Harris (1956).

Summary

A field investigation showed that the use of parathion-impregnated gauze strips for fly control in cowsheds did not affect the cholinesterase activity of erythrocytes (AChE) or plasma (BChE) in the farmworkers concerned, over a period of a month.

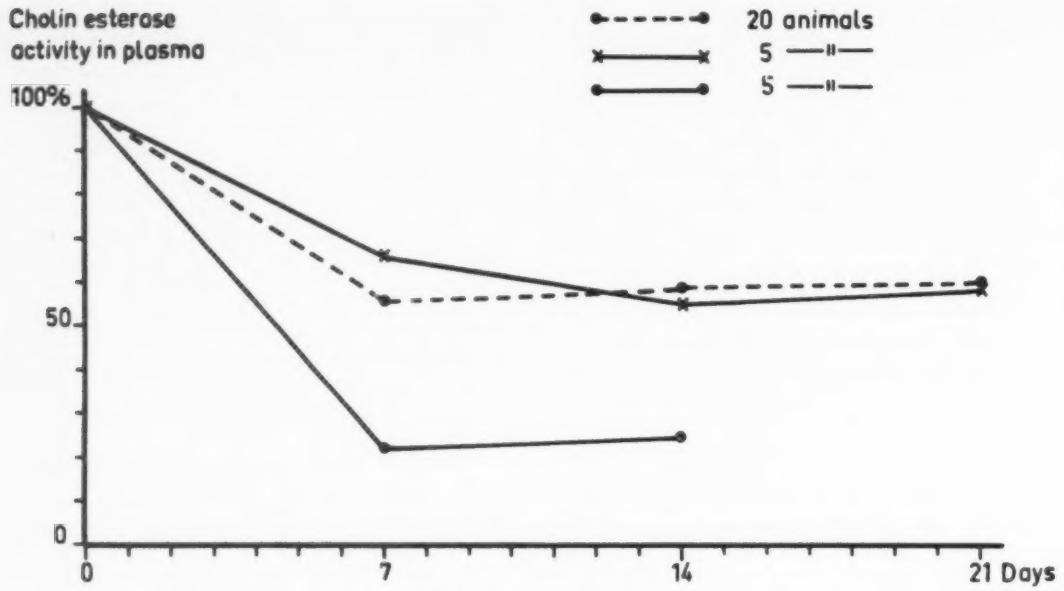


FIG. 5.—Effect on plasma cholinesterase activity (BChE) of prolonged continuous exposure. Temperature and ventilation varied in different experiments.

Laboratory experiments with guinea-pigs exposed to parathion-impregnated gauze strips at temperatures of 25° C. and above, and with a ventilation below 2·5 air changes per hour, showed that under these adverse conditions the plasma cholinesterase (BChE) activity was reduced. Erythrocyte cholinesterase (AChE) activity, which is small in guinea-pigs, was not estimated. The reduction in BChE activity was stabilized after seven to 14 days' exposure.

REFERENCES

Augustinsson, K.-B. (1948). *Acta physiol. scand.*, **15**, Suppl. 52.
—— (1955). *Ibid.*, **35**, 40.
——, and Heimbürger, G. (1953). *Ibid.*, **30**, 45.
Barnes, J. M., and Denz, F. A. (1953). *J. Path. Bact.*, **65**, 597.
Bidstrup, P. L., Bonnell, J. A., and Beckett, A. G. (1953). *Brit. med. J.*, **1**, 1068.
Cohen, B. S., Oberst, F. W., Crook, J. W., and Harris, C. (1956). *J. Pharmacol.*, **116**, 209.
Durham, W. F., Gaines, T. B., and Hayes, W. J., Jr. (1956). *A.H.A. Arch. industr. Hlth*, **13**, 326.
Fenton, J. C. B. (1955). *J. Path. Bact.*, **69**, 181.
Glömme, J., and Swensson, Å. (1955). *Svenska LäkT.*, **52**, 1175.
Kilpatrick, J. W., and Schoof, H. F. (1956). *Publ. Hlth Rep.* (*Wash.*), **71**, 144.
Maier, P. P., and Mathis, W. (1955). *Mod. Sanit.*, **7**, April, p. 32.
Wichmand, H. (1953). *Nature* (*Lond.*), **172**, 758.

MISCELLANEA

Health, Welfare, and Safety in New Zealand*

T. O. GARLAND

From the Occupational Health Unit, Central Middlesex Hospital, London

FIG. 1.—Old factories in Wellington, 1950.

I am frequently asked to give my impressions and views on health, welfare, and safety in New Zealand. There are severe limitations on generalizations of this kind; but during the last 10 years I have inspected over 1,000 different factories in New Zeland and other workplaces associated with mining, agriculture, timber felling, transport, and hydro-electric undertakings. From this experience certain general impressions have gradually crystallized.

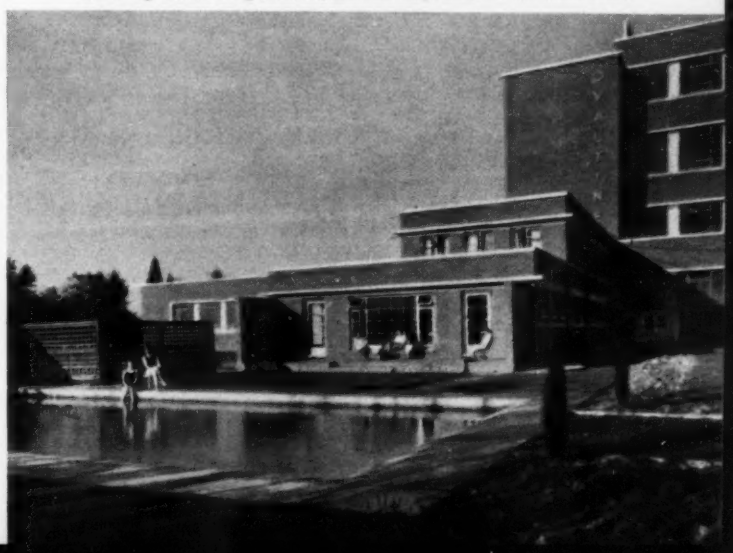
Industry in New Zealand is in small units and conditions on the whole are good. The minimum requirements for health and safety at work, as laid down in the Factories Act, 1946 (based on the British Act of 1937), are usually observed, and a substantial proportion of firms go far beyond these requirements. There is general agreement in this prosperous country that good working conditions are part of the share-out from the golden wool and the flow of milk and meat. Most employers are in business in a small way and are close to their workers.

The workers themselves, like other groups in the country, want, first of all, good pay—cash is good medicine. They seem, however, to be characteristically difficult to push around and, though prepared to work under bad conditions for high pay, they set very definite limits on just how bad the conditions may be and on just how long they will work under such conditions. Over the years a growing pressure on the part of trade unions has developed, here as elsewhere, for more welfare facilities and better provision for health and safety at work; but always their main drive is for higher wages—a policy in line with trade union tradition to raise the standard of living and to provide security for union members.

It is hard to say which authority is most influential in shaping attitudes to welfare in New Zealand. There is a well-established system of arbitration and conciliation between management and labour, which must be a big influence, but little high-level intellectual discussion on theories of personnel management comes either from the employers or trade unions. The pressure to conform to the law derives very largely from the State, through the officers of the Labour Department. The State, through conferences, for example, seems to initiate policy and shape standards much more than in Great Britain. When the civil servant comes forward with definite proposals he is able to do so in an atmosphere softened up by prosperity. Plenty of productive conflict arises over changes in conditions but at the same time there is an abundance of the goodwill which is always more in evidence when the belt is not pulled tight. Recently a National Safety Association has been formed, independent of the State, but it is not yet an appreciable influence.

The development of welfare services anywhere owes something to simple goodwill, the sense of affinity between members of the same social group. In former times there was often innate in the relationship of employer to employee a sense of the responsibility felt by the parent to the child. Simple goodwill, however, is not enough. I remember the bitter chagrin of an employer who bought an expensive type of helmet and airline and told a man that he must wear it in order to protect his lungs from some harmful dust. Later he came back to find the apparatus smashed to bits, with no one

FIG. 2.—Corner of modern factory containing canteen, rest rooms, and swimming bath, rose garden beyond and large lawn to the main road.



*Based on a paper read at the Duke of Edinburgh's Conference in 1956.

able to throw any light on how the damage had occurred. His goodwill was altogether too simple.

In any case, it is naïve to push the pure goodwill story very far. A potent force which encourages employers to provide health and welfare services is enlightened self-interest. Health and welfare pay. All books on good management say so, and in consequence:

> ". . . with to-day's competition for the most intelligent and efficient workers, stockholders cannot long afford directors who do not realize the importance of top health and safety conditions in their company's plants, nor managements which do not spend whatever money is necessary to give plant people the maximum of health and safety measures."—(GIBBON, 1947).

These sentiments, salted or ungarnished, can be heard in scores of speeches at conferences to-day, all over the world. Health and welfare thus become a technique for attracting and holding staff, much as the welfare state is a technique for keeping our whole society together. When labour is scarce welfare services also become an important item in competition between firms. In the later 1940s a firm in Auckland which employed mostly girls attracted much attention and some resentment by offering free hairdressing to female staff in working hours. Four hairdressers were included on the staff for this purpose.

There is often resentment towards pioneers of this kind from their peers; probably every move towards making working life more happy and comfortable has been widely resented by some section of the industrial community. " I'll have to give them all feather beds next ! " exclaimed one employer, exasperated by what he called unfair competition. How far can welfare go ? Certain American firms probably lead the field.

> " Among the features offered at various business houses which I visited were background music, movies during the noon hour, a terrace for suntanning, free tennis lessons, classes in interior decoration, personality development and horse-back riding, and social clubs that feature everything from bowling to dramatics."—(MCCORMICK, 1954).

It is unlikely, however, that mere material benefit, be it a haircut or a motor-car, will ever compensate an adult personality for the sacrifice of his own will and self-respect. Integrated adults may deliberately choose to work in a small, ill-furnished, poorly equipped establishment rather than in a large, highly organized, efficient one for the very good reason that they like being " someone " in the smaller place.

The elaboration of welfare imposed from the top means more organization and discipline of the individual —the extra comfort may be a trivial feeling compared with the sense of resentment engendered by being organized by others. The negative reaction of the child to mother's " I'm only doing it for your good " is also encountered by managements who treat their workers like children. Moreover, there is a wider implication. It is all very well to demand adult responsibility and self-determination from citizens who elect their rulers, but if the control and detailed organization of all movement and behaviour during working hours is extended to recreational activities, we are heading for social schizophrenia.

Motives easily become clouded; do we really want this or that, or do we just want the boss to pay out or the children to keep quiet ? Should we sometimes adjust our attitude towards welfare services by a little less " freedom from " towards a little more " freedom to ". One development I would like to see extended is to permit the use of factory premises and equipment on some cost-price basis for individual employees wishing to learn crafts out of working hours. More craftsmanship at the home level is one of the most creative potentialities of increased leisure. Certain industries, such as engineering, woodworking, and clothing, have an opportunity for permissive welfare here.

I would also like to see far more active and conscious appreciation of the importance of aesthetics. Stimulation from our senses strongly affects health and happiness, albeit we are largely unconscious of the stimuli. The reason we have survived at all biologically is that we have made the correct response to them. Are offices, factories, and workplaces to be made attractive ? What value should we put on colour, gardens, design of buildings, and furnishings ?

There is a feeling prevalent that industry should be shut away; it is unsightly alongside our dwelling-places. This aversion for everything pertaining to the workplace exists quite apart from the sound economics of zoning to facilitate service and supply routes, or the real need to shut away a noxious process. The attitude, surely, must be out of date. How much of it is due to unnecessary ugliness ? There are factories in New Zealand—admittedly a land undeveloped architecturally—that are among the best buildings in the country and set in grounds that challenge the many beautiful gardens around private homes or in parks. Why can't we live close to them ? Figures 1 and 2 illustrate this point. Talk to an average industrialist about aesthetics and he's likely to think you are crackers; talk to an average trade unionist and he's likely to think you are high-falutin. Modern industry should fill the gap left by the mediaeval Church as the patron of art as an alternative to ultra-violet lamps and hair-do's. If only a few more managers would lay out their own offices with a little taste and originality it would be something and I offer up a similar prayer for senior civil servants. What are we really working for ? Surely not solely for more production, for more imports, for more production *ad infinitum*.

There is plenty of scope for group participation (rightly a key phrase in industrial circles today) in this matter of aesthetics. A firm employing large numbers in somewhat scattered units was approached by the girls in one group to know if they could have the materials to re-decorate their canteen. For their part they promised the labour. The proposal was agreed. The result so pleased the management that they paid decorators to do the same in other canteens. In two years most of these were in a parlous state of wear and tear, but the one that the girls had decorated still looked in very good condition. Group morale is a fascinating study. Some industrial units do not seem to understand it at all.

An organization, large by New Zealand standards, at which nearly 2,000 were employed, was much concerned because obscenities were scribbled and drawn on the walls of their expensive new toilet blocks—not an uncommon phenomenon in many countries. A consultation between management and union officials, shocked into unity, agreed that less privacy would be a sound prophylactic measure and all the doors of the W.C. cubicles were removed. I would swear that any member of any of their families would have told them they felt better with the doors on.

Union officials often seem to be as much out of touch with the feeling of the rank and file as management are; by the very nature of their personal experience and background they are not often familiar with psychological theories or social science terminology. The lack of close contact is greater in the bigger organizations. One trade union representative demanded and received agreement on the provision of showers. After they had been installed, he shared with the manager the sense of hurt and lack of understanding that followed because nobody used them. It was not surprising, and resembled the story of the epic struggles to persuade miners in South Wales to use pithead baths. Yet all miners now use them. Showers in those factories where workers become hot and dirty will come to be as commonplace as baths in homes. Before long it will seem inconsiderate not to give any man the opportunity to go home feeling presentable and as clean as he arrived at work.

What is culture but this development and expression of feeling ? The function of any art is to stimulate our frontier of feeling to grow a little. To be effective the response engendered must link with experience and not be so intolerable as to threaten our integration, but the stimulus need not of necessity be merely pleasant and beautiful. However, it is essential to realize that the senses may grow tired or may be strained by too much stimulation or too much repression, just as muscles can be flabby or fatigued and torn. Satisfaction and tolerance can pass to boredom and unrest, which may progress to disgust and violent reaction.

The delights or the tensions and explosions that originate from the senses operate at work as in the home or anywhere else. While man is capable of considerable control and of the exercise of reason, his feelings cannot be disturbed too much or too long without basic instinctive reactions coming into play. Much more understanding is required of the importance of this factor in shaping occupational health. The effects of noise and lighting and colour at the workplace provide relatively simple examples of how physical health may be affected through the senses. Excessive noise may go further and become a clear physical danger to hearing.

I have pondered much on safety. Some of the confusion about safety policies lies in a failure to recognize a certain positive value in danger—safe for limb may be dangerous for mind and children should be allowed to climb trees and cross dangerous roads, thereby learning to deal with dangerous situations; but it is callous and irresponsible to let them pick up things they could not know were very hot, or fall into holes they have not yet learned about.

Every working group from a family to an army seems to have an accident rate. Possibly the best way to germinate an attitude conditioned to accident prevention is to sit around and talk with the people concerned. Group participation—no dogmatism—no censoriousness. But many times I have been asked, " For goodness sake, don't go about and put ideas into their heads ", when I have wanted to discuss hazards with the men concerned.

It is possible to draw a line between danger which is emotionally stimulating on the one hand and plain foolhardiness on the other. Sir Arnold Toynbee has said that civilization owes much to the former and that safety first on every occasion could be socially disastrous. Safety first is out of date as a slogan, in any case.

Powerful resistances against taking care lie deep within us. I meet them in myself and in my own sons and they seemed to me to be particularly evident among New Zealand men. They have a maddening phrase " she's right " which is constantly used to denote a sense that things are not really quite right, but that they will do. (In Oxfordshire when a hay wagon was fully loaded, the pitcher used to shout to the man on top: " her'll do ". He meant just what he said.) The firm may provide goggles and guards, helmets, and local exhaust ventilation, but the workers will not always use them.

The trade union representative complains as strongly as does the foreman, the works manager, and the managing director, but how do these higher paid men themselves behave ? Suggest to any one of them that he smokes less for health, that he diets more wisely, that he does not drive his car so fast, that he plays safe. Does he do it ? In our society, professional men, business men, skilled workmen and unskilled all seek more money or prestige before better health; they seek emotional satisfaction before safe practices. Perhaps this attitude is more socially healthy than at first appears. Social health is certainly not always synonymous with individual health; nor is being secure the same as feeling secure. Do the group and the individual clash again here ?

It is uncertain who is to be the disciplinarian in safety matters. Authoritarianism is out of date; it is inefficient, for it fails to use the potential of collaboration. Leadership remains a modern requirement. I have seen managers over and over again tolerate stupid, illegal, and dangerous practices knowing them to be so but seemingly at a loss to say or do anything; and I have seen trade union officials behave likewise, and inspectors, and have done so myself.

I have heard a works doctor say, " It's not my business to see that the men wear goggles; that's management." Many a manager I have heard say, " I can provide them, but I can't make them wear them." No participation again. In some circumstances a severe discipline is possible, but the threat of dismissal, like the threat of being shot in the army, has limited application. The limit is very quickly reached in New Zealand and a walkout results. It seems that every now and again one side or the other must stick its toes in and have a showdown and some strife occasionally is no justification for gloom and despondency. Both management and labour are in need of specialist advice, from medical men and also, I

think, from social scientists on what contributes to prejudice, on the source of unconscious direction, be it from tradition, peer groups, or elsewhere, and on likely chain reactions from particular measures.

Possibly there will gradually be a movement towards industrial democracy, using the term as defined in the pamphlet issued by the Progressive League (1956). Democracy is a confusing word recognized as desirable in state affairs but highly suspect still in industry, private and nationalized. Some interesting experiments far in advance of co-partnership, profit sharing, joint consultation, and similar arrangements, are now going on in Great Britain, France, Italy, and West Germany.

I want to see people more capable of being responsible for their own health and safety. Seeking opportunities and perfecting techniques for teaching should occupy doctors in industry far more than routine examinations and clinical medicine.

Occupation can and ought to be extremely health-making, mentally and physically. It is noteworthy that occupational therapy first started in mental hospitals. Already, in the big and successful industrial concerns, physical dangers are to a great extent guarded, fumes and dusts trapped and sucked away, good hygiene and amenity standards assured. The position is very complex, for more production is socially healthy, when achieved without dangerous tensions.

Medicine should move further towards affecting our way of life, our social organizations and institutions, even though at present medical training does not encourage an understanding of social disciplines. The doctor is taught primarily to be technically adept at diagnosis and treatment of the individual and that is how he is mainly used in industry as elsewhere. The accent on clinical medicine within the factory should not become too strong, especially when it duplicates an outside service. In my opinion, the doctor should be drawn more into shaping the working way of life, with an educative rather than a directive function. Some clinical service, of course, is necessary, varying largely with the type of work and geographical situation. Apart from the time factor, and some doctors rarely have time to go round their factory, the industrial doctor should beware of the assault on the individual which is entailed by compulsory examinations and treatments. There is a far greater danger in the offing than that of missing some significant symptom—

> The whole earth is our hospital
> Endowed by the ruined millionaire,
> Wherein, if we do well, we shall
> Die of the absolute parental care,
> That will not leave us, but prevents us everywhere.
> (T. S. ELIOT, East Coker.)

Here and there in my own confusion there are spots of light. Health, welfare, and safety appear an indivisible trinity within a broad conception of health that is very much undervalued. This is as evident in the senior executive who would rather be a success than avoid an ulcer, as in the labourer who would rather have dirt or danger money than adopt a self-discipline of clean and safe practices. The same attitude exists in doctors and other professional men.

Within the industrial framework there are undoubtedly factions antagonistic to one another—not just two factions—which find themselves at loggerheads in this field as elsewhere. Techniques for understanding these differences need to be developed by social science studies, statistical analyses, feed-back techniques, and so on.

Leadership calls for consideration of the point of view of the led. If compromises are reached which appear silly to a professional man—one that always irritates me is the acceptance of milk as a universal prophylactic—it does not greatly matter. He, too, must often appear silly. Any compromise which is arrived at by genuine collaboration does much to hold the group together. We must be sensitive both to the pressure for change, and to the necessity for stability. We have to keep moving, for nothing is concluded:

> . . . so there's to be
> No climax and adorable close
> With ego agonistes crowned and smiling ?
> The strange charm of being alive breaks off
> Abruptly, with nothing determined, nothing solved,
> No absolute anything . . . .
> . . . . . .
> How nature loves the incomplete. She knows
> If she drew a conclusion it would finish her.
> But, oh God, for one round Amen.
> (CHRISTOPHER FRY, *Venus Observed*, Act 2, Sc. 2.)

REFERENCES

Gibbon, W. B., Jr. (1947). Address to Industrial Hygiene Foundation, Pittsburgh, November 20, 1947.
McCormick, Elsie (1954). Independent Woman, 33, 9.
Progressive League (1956). Report by the Occupational Democracy Group. *Democracy in Our Working Lives.*

OBITUARY

Ludwig Teleky

Industrial medicine has lost a leading international figure and a beloved fellow-worker through the death of Dr. Ludwig Teleky. He was born in Vienna, the son of Hermann Teleky, M.D. He died in the Jewish Memorial Hospital, New York, on August 20, 1957, aged 85 years.

He was lecturer in social medicine in the University of Vienna from 1909 to 1919. From 1919 to 1932 he was Director of the Postgraduate Academy of Public Health and Industrial Medicine at Dusseldorf, and at the same time Medical Inspector of Factories for the Rhineland, and a member of the Central Council for Health in Berlin. In 1932 in the Nazi persecution of the Jews he was deprived of these appointments and returned to Vienna.

He was a founder member of the Permanent International Commission on Industrial Medicine in 1906, and in 1951 was elected an honorary life member of the Commission in recognition of his eminence.

Teleky attended the 8th International Congress on Industrial Medicine at Frankfurt in 1938. This Congress was interrupted by the Munich crisis and the delegates dispersed. It was necessary for Teleky's safety for his friends to get him over the border into Switzerland. Friends in Austria and America then arranged for him to go to the United States of America, where he was appointed to a lectureship in the University of Chicago, which he held from 1939 to 1944.

In 1944 Dr. Leonard Greenburg, now Commissioner of the Air Pollution Control Department of New York, invited Teleky to work with him in the Labour Division of the New York State Department of Industrial Hygiene.

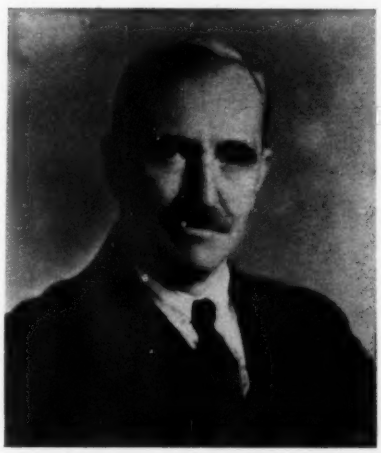
While in New York Teleky devoted much of his time to writing and from his pen flowed many articles and a number of books upon occupational health. He edited the Encyclopaedia of Industrial Diseases published by the International Labour Office. His book " The History of Factories and their Hygiene " was published by the Columbia Press in 1948, and "Gewerbliche Vergiftungen" was published by Springer-Verlag, Berlin, in 1955.

The Grand Cross of Merit was conferred on Dr. Teleky by President Heuss of the German Federal Republic, and in 1952 in a new part of Hamm, one of the ancient Hanse towns of Germany, a street was called by his name.

His wife died in 1953. He is survived by two daughters, Anna, a worker in social medicine now living in Vienna, and Agnes, a Doctor of Philosophy of the University of Frankfurt, who is engaged in social science work in London.

T. E. A. STOWELL

Professor E. L. Collis, C.B.E., D.M., M.R.C.P.



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Professor E. L. Collis, Emeritus Professor of Preventive Medicine in the University of Wales, died in hospital at Forres, Morayshire, on October 1, 1957, aged 86 years. By his death Great Britain has lost one of its pioneers of industrial medicine.

Edgar Leigh Collis was born at Stourbridge on November 25, 1870, the son of W. B. Collis, J.P. From Stourbridge Grammar School he went on to Charterhouse, and then to Keble College, Oxford. A notable sportsman in those days, he was president of the Oxford University Swimming Club and represented the university in athletics against Cambridge in 1892 and 1893, tying for first place in the hurdles in the latter year. After gaining first class honours in the Natural Science School at Oxford he went to St. Thomas's Hospital for his clinical studies, qualifying in 1896 and graduating B.M., B.Ch. in the following year. He proceeded to the D.M. in 1919, and became M.R.C.P. in 1920. For the first 10 years or so of his professional life he was a general practitioner in Stourbridge, where he was certifying factory surgeon and on the staff of the Corbett Hospital.

In 1908 he joined the staff of the Factory Department of the Home Office as a medical inspector of factories, and soon became a leading authority on pneumoconiosis, the subject of his Milroy Lectures in 1915. He had also made various investigations on behalf of Home Office departmental committees, including the study of heat stress in hot industries.

When, early in the first World War, the Minister of

Munitions set up the Health of Munition Workers Committee, Collis was appointed a member of it, and in 1917 he became Director of Welfare and Health in the Ministry.

Collis and his colleagues on the war-time committee were convinced of the pressing need for the application of physiological science in industry and recommended that when the war ended some arrangements should be made for continuing studies such as they had initiated. As a result of that recommendation the Industrial Fatigue Research Board was set up in 1918 and Collis was one of its first members. In that capacity he was able to advise on the organization and direction of research into the physiological and psychological problems of industry.

In 1919 he was appointed Talbot Professor of Preventive Medicine at the Welsh National School of Medicine at Cardiff and there he continued his studies of pneumoconiosis and took an active interest in the improvement of working conditions in coal-mines and in miners' welfare. At about this time he became a member of the Miners' Welfare Commission on which he served for over 30 years.

By this time Collis had an international reputation as an authority on industrial hygiene. From 1922 to 1936 he was British Editor of the *Journal of Industrial Hygiene*. In 1924 he gave the Harben Lectures on " Phthisis and Industrialism ", and in 1926 he gave a course of lectures at Harvard University. He was co-author with Professor Major Greenwood of the book " The Health of the Industrial Worker " which was published in 1921.

Professor Collis retired from his university appointment in 1933 and was made emeritus professor. He went to live in Lossiemouth, Morayshire, where he became a Justice of the Peace. In 1937 he was appointed C.B.E. and in 1954 the Society of Apothecaries conferred on him the Diploma in Industrial Health, *honoris causa*. He never lost his interest in industrial medicine and in spite of his advanced age he was a regular contributor to the *Bulletin of Hygiene* until the time of his death. During the last war he served as a medical officer in the Home Guard and was appointed Lieutenant-Colonel when he was about 70 years of age. This appointment gave him great pleasure and considerable amusement.

From 1919 to 1921 he was my Director and thereafter we kept in close touch with each other until several years after he had retired from his chair at Cardiff. Collis's wide knowledge of industry made him a particularly valuable adviser on field investigations, and a discussion of one's problems never failed to bring stimulating suggestions from him. He was kind and considerate and always ready to advise a junior worker. He was a good critic and his criticisms were always constructive. He was intensely interested in the human problems of industry and his earnestness was tempered by a keen sense of humour. Besides being educative, work with him provided many amusing moments.

He married Barbara Shields, daughter of Principal Fairbairn, of Mansfield College, Oxford, and she survives him.

His passing will bring deep regret to all those who are fortunate enough to have known him.

THOMAS BEDFORD

BOOK REVIEWS

Principles of Epidemiology. By Ian Taylor and John Knowelden. (Pp. vii + 300; 26 figures. 30*s*.) London: J. & A. Churchill. 1957.

For a long time our ability to control infection has depended upon how well we understand the complex patterns made by disease in the community. The controlled observation of these patterns has come to be known as " epidemiology " and the techniques used as " epidemiological ". In the past, therefore, knowledge of epidemiology has been of importance mainly to those concerned with community health and particularly with the control of infectious disease. Not very surprisingly, epidemiological techniques have helped us to understand other non-infectious diseases where the principal clues to aetiology have come from their geographical, social, or occupational distribution. This understanding has been of benefit particularly to industry but there can hardly be any part of medicine where epidemiology in its new and inevitably broadened sense is not in current use. For this reason the techniques used by epidemiologists are now of interest and importance to us all; they are among the essential tools of all scientific medicine.

Because epidemiology is almost the only part of medicine without an elementary text-book we have looked forward for some time with special interest to the two or three books on the subject which have been promised. If this book, which is the first to appear, is any measure of later quality we are to be fortunate indeed, for Drs. Taylor and Knowelden have given us a most useful and interesting introduction to the subject.

The increasing breadth of epidemiology has set the authors a problem of presentation. They have compromised by giving the first and last parts of the book largely to general principles and the centre piece, the main part of the book, exclusively to the infections.

A consideration of the ways of measuring disease, the sources of information, and the problems associated with collecting mortality and morbidity statistics leads on to the use of rates, to the characteristics of populations, and to the census. There is a clear and interesting discussion of the use of special survey techniques with examples in the fields of general practice and industry and a note on prospective studies of the type used recently in the investigation of lung cancer. Finally in the introductory chapters, there is a discussion of the structure of the controlled study and of the difficulties in selection of the control group.

From this exciting beginning (which is surely much too short) we are taken on a brief course of bacteriology and virology as an introduction to the characteristics of the classical air-, food-, water-, and milk-borne infections. A section on immunity leads to a description of current immunological techniques. Finally, slipping away again from orthodoxy the authors return to an all too brief consideration of the measurement of " host " factors in epidemiology ranging from age and sex through the family, the place of living, housing, neighbours, occupation and social class. References are always given in footnotes, which is convenient as one reads the text, but is a minor frustration when a group of references is needed.

Here is a book which is both satisfying and a little disappointing, satisfying in that it fills an important gap among our textbooks and is clear, concise, and well produced; disappointing only in that it whets the appetite for more, for the principles of epidemiology applied to the new threats to the public health, to duodenal ulcer and coronary disease, accidents, and damaged genes. Let us hope there will soon be a Part II to this excellent book.

E. M. Backett

Le Précis de **Médecine du Travail,** 2nd ed. Edited by Professeur C. Simonin and others. (Pp. xii + 1,406; 326 figures. Fr. frs. 6,800.) Paris: Librairie Maloine. 1956.

This is the second edition of a systematic text book, first published in 1950, on occupational medicine, edited by Professor C. Simonin, director of the Institute of Legal and Social Medicine at Strasburg. Professor Simonin himself contributes many chapters, and his 27 co-authors come mainly from the Strasburg school. The first edition was awarded the Prix Fournier of the Académie Nationale de Médecine and it is clearly worthy of the distinction. The new edition contains 32 new chapters, which deal, amongst other subjects, with the psychology and physiology of work, toxicology, systematic and special pathology of occupation, and the duties and remuneration of works doctors. The book has over 300 illustrations, of which nearly 200 are new; the type is clear, but the text is printed in two sizes, which does not make for easy reading. This suggests the necessity for a new paragraph on occupational eye-strain in the readers of text-books on occupational diseases !

France has been a backward country as far as industrial health services are concerned, but in 1946 a compulsory national industrial health service sprang Minerva-like fully armed straight from Jupiter's head. The doctors engaged in the health service have to do a year's course in occupational health and pass an examination for the Diplôme de Médecine du Travail. This book covers the syllabus for the examination, and it is indeed formidable. Our own candidates for the D.I.H. have to know a great deal less. It is interesting to note that both works

doctors and the medical inspectors of factories, of whom there are about 45, hold the diploma.

The authors admit that, up to the present time, France has not paid as much attention to the working environment as it deserves, and that in particular, the equipment and number of industrial hygiene laboratories are scanty. They have a great need of chemical toxicologists.

Their organization of occupational medicine is concerned essentially with the individual, and that, they admit, is not enough, because it is the working environment which provides the health risks. In comparison with the Americans the French are in the lead as far as " medical prevention " goes, but they lag behind as far as the organization of industrial hygiene is concerned.

Much attention is given in the book to American publications, as well as French and German, but little reference is made to British experience and results. It almost seems as if the authors are able to read American English rather more easily than English English. No attempt, however, is made to give a complete bibliography on any subject, but the student is given a list of journals, books, and articles which he might study with profit. In the information given about many subjects there are noticeable gaps. In the short paragraph, for instance, on poisoning by tetra-ethyl lead, no mention of acute mania is made, and the sections on vanadium and cadmium poisoning are out of date. The article on beryllium poisoning is conventional and adequate but it mentions that in the chronic forms a mistaken diagnosis of silicosis might be made, especially if the worker has inhaled a mixed dust containing silica and beryllium. The possibility that in fact there might be silicosis as well in these cases is not entertained, and on this aspect the authors have closely followed American opinion on the subject.

The volume is divided into four main sections, the first three dealing with the psychology, physiology, and the pathology of occupations, and the fourth with the protection of workers. But an interesting introductory series of articles puts the stamp on the character and philosophy of the whole book. The editor, Professor Simonin, discusses why and how the health of workers should be protected and then gives in bold type the factors which go to make up the doctrine of occupational medicine, which reads like the Atlantic Charter. It stresses the importance of the individual as opposed to the economics of production and the fact that occupational medicine helps men to live and does not only prevent them from dying. M. Gaudiot, a divisional inspector of labour and manpower, deals with the organization of work and the nature of industry in France, as well as giving concise descriptions of the Bedaux system, Taylorism, Stakhanovism, and the administrative doctrine of Fayol.

The main part of the book is didactic and systematic, and as such is suitable for students preparing for an examination. The diseases of many occupations are dealt with fully, and one chapter of special interest is that describing the occupational risks of workers in rural surroundings. Another chapter is concerned with the building industry, public works, and road construction. Still another deals with the risks of workers in hospitals. In fact, it would be difficult to find a text-book in any language which takes such a wide sweep of occupations. The only comparable one in this country is " Diseases of Occupations " by Dr. Donald Hunter.

To those who are interested in comparing systems of occupational health services in various countries the brilliant series of chapters by M. Gaudiot on the law relating to protection of the workers will be of absorbing interest; and doctors in this country will be particularly interested in his description of the administration of the new national industrial health service and where the doctors fit into it. As with all things French, there is a ruthless logic and commonsense about the whole organization which is highly attractive. It would be interesting to know how the scheme is working in practice, but even if after 10 years there are still growing pains, other countries could learn a great deal from it.

A. I. G. McLAUGHLIN

The Diseases of Occupations, 2nd edition, enlarged and revised. By Donald Hunter. (Pp. xvii + 1,100; 447 figures. £5 5*s*.) London: The English Universities Press. 1957.

It is a tribute to the author of an expensive book about an esoteric subject that it should reach a second edition only two years after it was first published. Those who were enchanted by the first edition will not be surprised at this outstanding success.

In the new edition, certain corrections have been made and the index has been improved. New sections have been added on thallium poisoning, iron and steel foundries, the hazards of working in sewers, and on the National Coal Board Medical Service. Some sections have been brought up to date, for example, those on vanadium, manganese, and cadmium poisoning. A few pages on vital statistics and epidemiology have been added to the chapter on social reforms in the nineteenth century but the modern uses of epidemiology in industrial medicine are not described, and some important results of recent research are not included. There is still no mention of the results of recent researches on bladder tumours in dye-stuff workers, on the risk of lung cancer in asbestos workers, or on the epidemiology of coal-workers' pneumoconiosis.

The statement that almost all new workers in cotton mills suffer from mill fever or cotton cold, is not true today, although it may have been so half a century ago.

Thomas Legge's " Industrial Maladies ", published more than 20 years ago, and not since revised, is a classic which should still be read. Donald Hunter's book is in the same class but its value as a work of reference would be enhanced if it were made more up to date by including the results of recent research, many of which are conveniently collected into the volumes of the *British Journal of Industrial Medicine*.

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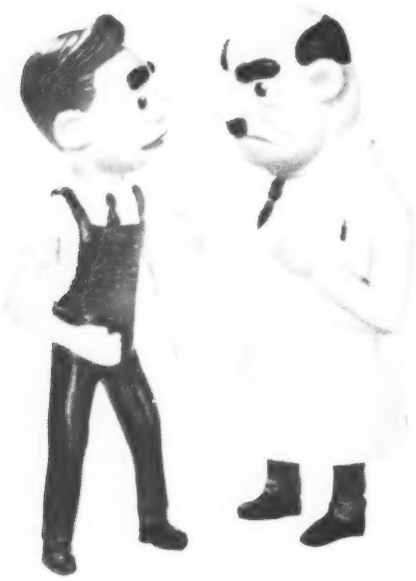

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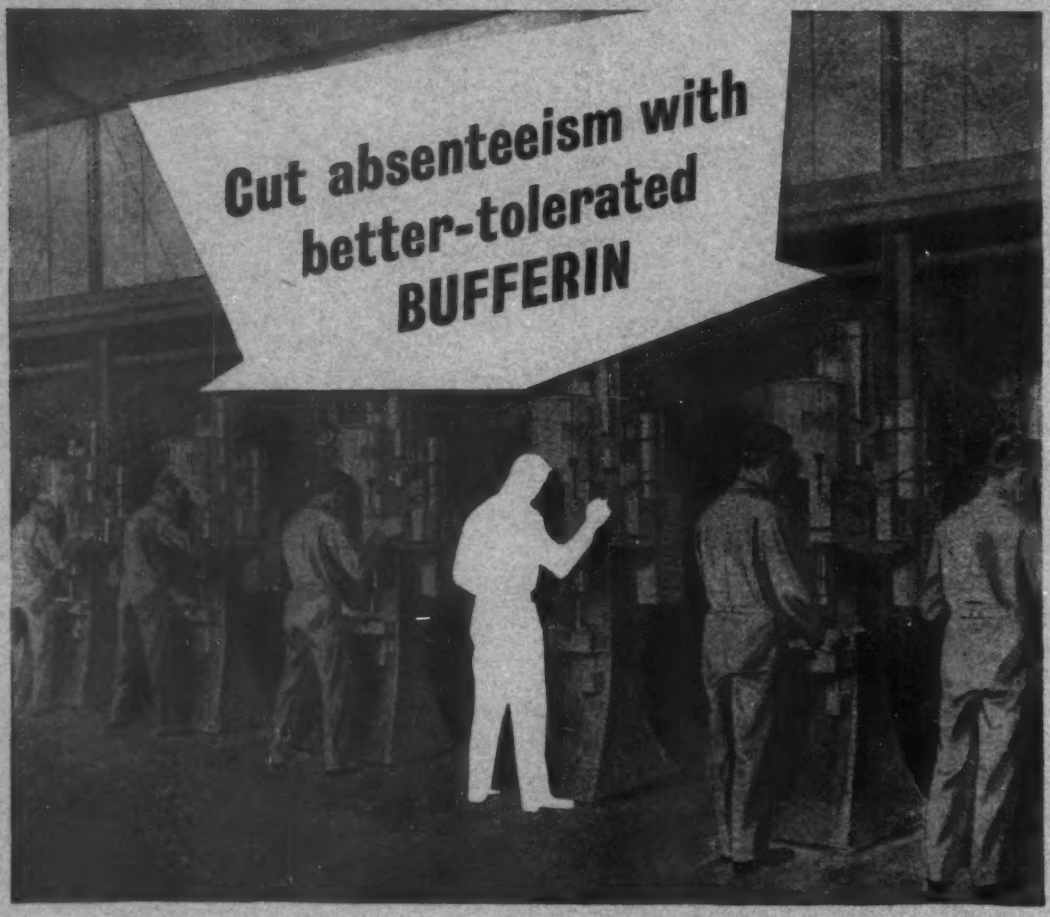

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